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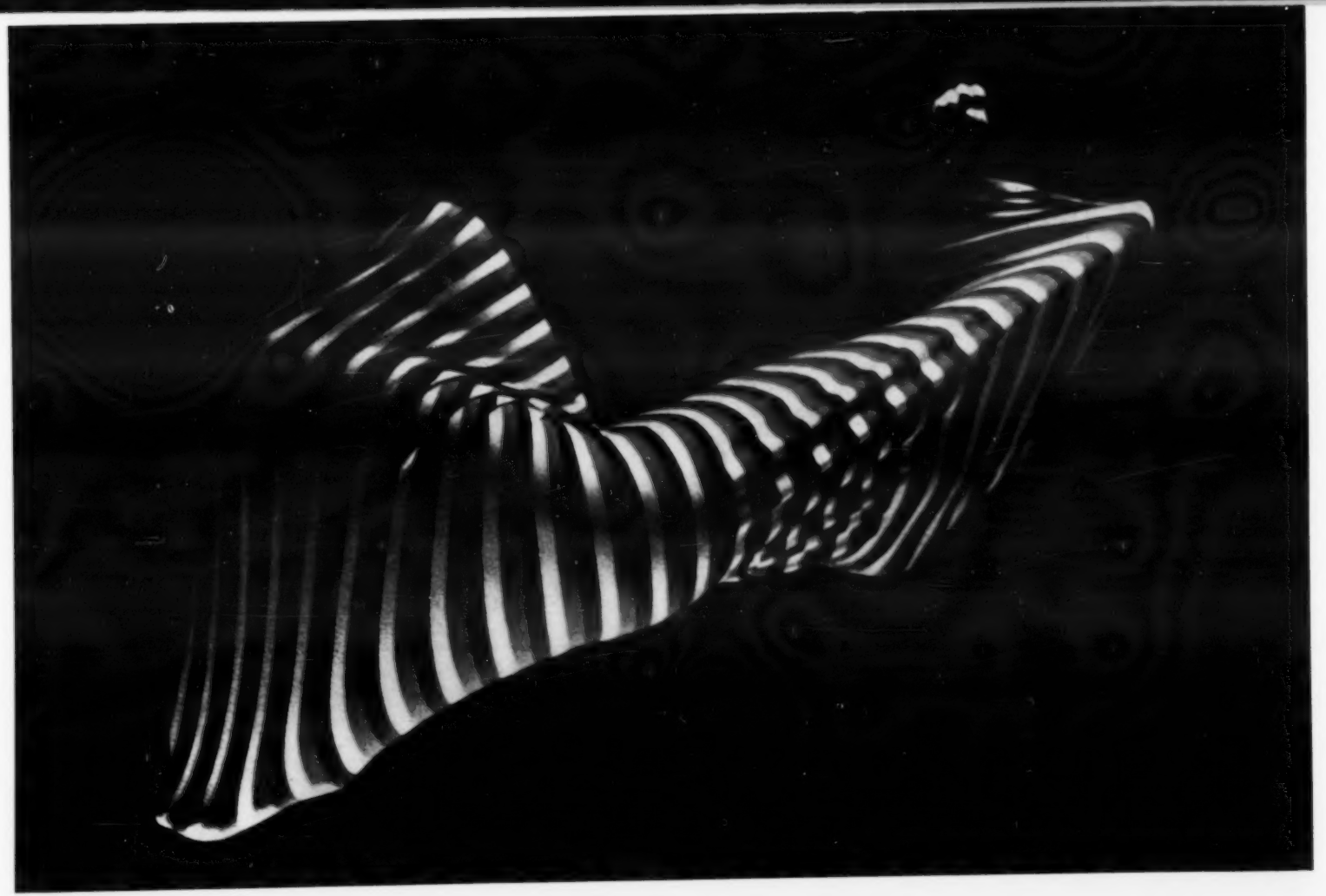

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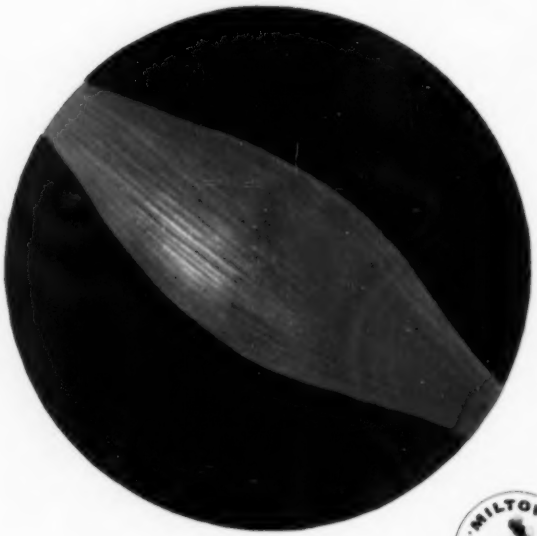

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Recent Memory Impairment in Unilateral Temporal Lesions

A. EARL WALKER, M.D., Baltimore

Introduction

In recent years a physicochemical basis for neuronal memory patterns has been hypothesized on the basis of intracellular reversible protoplasmic reactions.[10] This thesis explains satisfactorily the perception of sensory phenomena in the primary cortical areas. However, there is increasing evidence that many perceptual analyses are formulated in cortical or subcortical neuronal circuits other than primary sensory centers.

One of these cellular constellations important in certain memory processes would seem to be related to the temporal lobe. This has been demonstrated both in experimental animals and in man. Recent experimental studies in monkeys have revealed defects in visual discrimination due to damage to the inferior temporal cortex. This deficit is greater in visual learning than in retention of old visual habits, a finding which might be construed as representing an impairment in visual recent memory.[1]

In man, the evidence that the temporal lobe plays an important role in memory processes is quite impressive. During surgical procedures upon the epileptic brain, Penfield[7] induced memories by electrical stimulation of the superior and lateral surfaces of the temporal lobe in approximately 25% of cases. Excision of these areas does not abolish the memory. On the other hand, stimulation of the medial temporal structures, which may produce automatisms and bizarre behavior, well described by Feindel and Penfield,[3] is accompanied not only by amnesia of the ictal phenomena but also by a loss of memory during a period, before and after the attack, of overtly normal conduct. Bilateral lesions of the medial temporal structures, Grünthal,[5] found, produced severe memory impairment, a report which has been confirmed by another case studied by Glees and Griffith.[4] Scoville[8] observed grave loss of memory in two patients following bilateral excision of the medial temporal structure for a distance of 8-9 cm. from the temporal tip. Unilateral temporal lobectomy may be responsible for amnesia, for Penfield[7] states that "in occasional cases there is distressing memory loss," and Scoville[8] briefly refers to two patients who had grave memory disturbances after inferior temporal lobectomy.

Recently Milner[6] has examined psychologically two of Penfield's patients with memory loss following unilateral ablation of the dominant hemisphere. Psychological examinations showed that the memory loss was quite selective, for the general intelligence, old skills, and remote memory remained intact. Yet little could be remembered of recent events.

In a personal series of temporal lobectomies for epilepsy severe memory impair-

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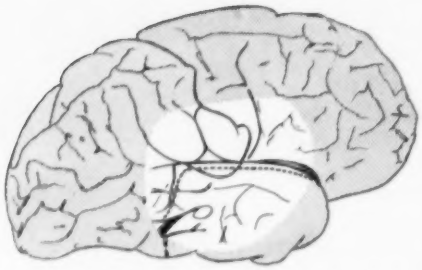

Fig. 1 (Case 1).—Sketch of the right hemisphere as drawn from a photograph of the unshaded area made at the time of operation to show the site and extent of the temporal lobectomy, indicated by the interrupted line.

ment has been encountered in three patients. The condition is not necessarily associated with an epileptic diathesis, for the syndrome occurred in a fourth case in which the temporal lobectomy was for exposure of an aneurysm.

Report of Cases

Case 1.—A 53-year-old, right-handed man was referred because of epileptic seizures, which he had had for 19 years. In his first attacks he would get up, turn to the left, and fall. During the first eight years the attacks occurred about every six months, then about once a month, in spite of phenobarbital and diphenylhydantoin (Dilantin) therapy.

The patient had no warning of the attack, and only knew he had had an attack because of soreness in his arms. Occasionally he had cut his face or scalp in a fall. His attacks were variously described by his sister, who thought that at times she "could talk him out of one." If, however, he was restrained, he fought. Apparently, in most attacks, after the initial period of bizarre behavior, he had a generalized seizure; one attack witnessed by Dr. J. K. Quattlebaum was described as follows:

"When lying quietly in bed, he suddenly jumped over the side-rails, ran around to his drawers, and began searching through them. He picked up a magazine, got back into bed, read for two minutes, and again got out of bed and began to drool at the mouth. Gradually he went into a generalized clonic convulsive seizure. Ten minutes later, although confused, he declared he felt fine."

On physical and neurological examinations, no significant abnormalities were noted. Roentgenograms of the skull were reported as normal; a right carotid angiogram and pneumoencephalogram, after replacement of 200 cc. of spinal fluid with air, were also normal.

An electroencephalogram on Sept. 6, 1951, was reported as having a right temporal slow-wave focus, and a sleep record the following day brought out a spike focus in the right temporal lobe.

On Sept. 14 a right temporal lobectomy was performed, the anterior 7 cm. of the lobe being ablated. The ablated lobe measured 7×4×3 cm. and weighed 36 gm. The pathologist reported sections as normal cortex.

The patient regained consciousness but was restless and combative. On the third postoperative day he was drowsy, and the following morning he was taken to the operating room and, with thiopental (Pentothal) anesthesia, the wound was reopened. An extradural clot 2-3 cm. in thickness and a smaller intradural clot were evacuated. No bleeding points were found. After this procedure the patient had an uneventful convalescence and was discharged nine days later.

On Nov. 4, 1951, the patient was found tearing up his bed and breaking glasses and lamps. He took everything out of the Frigidaire and then attempted to go outside in his underwear. He was restrained and shortly regained consciousness.

Following the episode he returned to his newsstand and had no trouble until Feb. 23, 1953, when he was found in coma on the street and taken to a hospital. For two months he was very confused, and even in May, 1953, he could not find his way about his home. When seen on Oct. 20, 1953, he had had no further attacks, but his memory was so bad he could not get articles from the store. His sister described his condition thus:

"Each day I notice that his memory is weakening. He will tell me the same thing over and over. And he forgets things that I will ask him to do for me—something to keep his mind occupied. I will have him go to the store to get my groceries, and he would always forget several items; so I now make a list for him. I put him through these tests to see how he reacts. While he does not have the seizures as he used to have, he never seems to feel well, and is so depressed at times. This is not his natural mood at all, as he was always so happy and cheerful. He just has no ambition, sleeps long hours, and naps all through the day. He is not able to work any more—and remains home. This worries me, too, as I am in constant fear that something might happen at the house, a fire, or something that he will forget. Several times when I arrive home at 5 p. m., I find the electric coffee pot still connected, and when I ask him how long it has been on, he cannot tell me—of course, it is always HOT—and this week he forgot to turn off the water in the bathroom, and it had soaked through the walls when I arrived home."

In this case it is difficult to ascertain the precise anatomical basis of the responsible lesion, for he seemed to have no memory impairment after the temporal lobectomy for over a year. It may be presumed his amnesic state was ushered in by a psychomotor attack, but whether this was associated with a vascular lesion is not known. Hence this case will be pursued no further.

CASE 2.—A 57-year-old, right-handed housewife was referred by Dr. Charles Wainwright because of black-out spells of nine years' duration. Her past history was not significant except for a fall from a horse at the age of 4 years, when she was unconscious for eight hours. Nine years previously, just after her menopause, she began to have "weak feelings," which were described as short lapses in her stream of consciousness and activity, in which time she might lick her lips or have a feeling of fear. One year later she began to have generalized convulsions without warning, with a postictal period of confusion. Some of these episodes apparently consisted of periods of bizarre behavior, of which she had no knowledge. In one, she suddenly climbed over the sides of her bed, then clambered back, and pushed against the bed sides with hands and feet until she knocked one down, upsetting a lamp. She firmly grasped the other bed side and would not let go. She vigorously chewed gum but was unresponsive. Within a few minutes she regained consciousness and had no memory of the episode. In another episode, she got out of bed, drooling at the mouth, paced the floor, and opened and closed dresser drawers as if searching for something. Then she walked into the hall, back into the bathroom, threw open the windows, and gazed out. When spoken to, she made no reply. Then, as she appeared to be coming out, she replied to a question, "I cannot hear you," although she correctly responded a minute later. When the attack was over, she had no memory of it. In spite of anticonvulsive medication, she was having attacks every month or two.

Physical and neurological examinations were normal. On Oct. 16, 1951, an electroencephalogram was reported by Dr. Curtis Marshall as showing an abnormal amount of slow activity in the temporal leads. A second record with the patient awake showed a slow-wave focus in the right temporal region with random low-voltage spikes and sharp waves. In sleep this same area gave rise to high-voltage isolated spikes, reversing at the tip of the right temporal lobe.

A right carotid angiogram was reported normal.

On Oct. 26, 1951, the tip of the right temporal lobe was removed 6 cm. from the temporal pole. The uncus and amygdala were removed by suction. Because spiking was still present posterior to the vein of Labbé, a subpial dissection of the first and second temporal convolutions was carried out for 2 cm. This eliminated the spiking, and the wound was closed in anatomical layers.

The specimen measured 4×2.5 cm. and weighed 15 gm. Histological examination was reported as showing normal cortex.

The patient had two brief generalized seizures the morning after operation and then no further attacks prior to the time of her discharge.

In the first postoperative days the patient was confused and talked somewhat incoherently. In a few weeks this mental disorientation cleared, to leave a residual memory impairment and constant euphoria. On one occasion, accompanied by her nurse, the patient went to the "Dime" store. While the nurse was making some purchases, the patient picked up several articles which she did not need and discovered that she had no money with which to pay for them. While the nurse was straightening up this transaction with the clerk, the patient wandered to another counter and repeated the same performance. Aware of the defect in the memory, the patient was constantly on guard and refused to allow any testing of it, cleverly circumventing all questions which might reveal her disability.

On Sept. 12, 1952, she returned to the hospital. In the interval she had had two or three minor attacks and one major episode, on April 29, 1952, when she decreased the amount of phenobarbital she had been taking. She had had no psychomotor episodes.

She maintained that she could think as well as ever and that her memory was fine. However, when given a paragraph to read, she was unable to repeat the context, or even to give the subject of the material within two minutes. As soon as this became obvious, she refused any more testing, and would not permit a formal Wechsler-Bellevue examination on the next day.

Neurological examination, however, was normal. An electroencephalogram on Sept. 17, 1952, was

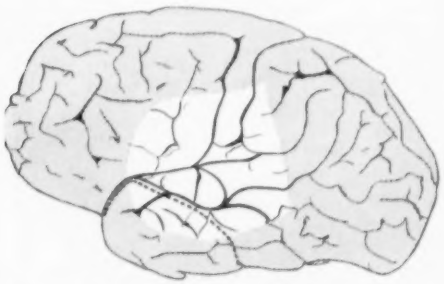

Fig. 2 (Case 2).—Sketch of the left hemisphere showing the extent of temporal ablation, as indicated by the interrupted line.

reported by Dr. Curtis Marshall as showing left temporal slow random activity with a spike focus in this same area.

The patient has been free of attacks and returned to her position in charge of a large store. According to her physician, she seems to have no memory of disturbances, although no formal testing was performed.

In this case the temporal relationship of the lobectomy and the memory loss is quite evident, but it is unfortunate that the patient refused to cooperate in psychological testing. Yet this refusal is in itself evidence that the patient was aware of the defect, for she was quite agreeable to any other type of examination.

It seems probable that the impairment of memory has cleared to a considerable extent, if not completely, since the patient appears to be managing a large store without difficulties.

Case 3.—A 40-year-old, right-handed man was referred July 7, 1952, because of seizures. He was seen on the psychiatric service to which he had been transferred because of irritability and combativeness upon admission to the medical wards. His history was difficult to obtain, but he stated that he had had seizures as a child and for about 12 years had suffered unconscious spells and periodic confusion, when he had no recollection of his actions. For some time his "seizures" were initiated by a peculiar dysesthesia in his left foot.

What could be obtained of his previous medical history was neither reliable nor significant.

On physical and neurological examinations no abnormalities were noted.

An electroencephalogram on Feb. 19, 1951, was reported by Dr. Curtis Marshall as showing random low-voltage slow activity in both temporal regions. On July 15, 1952, a consistent left temporal spike focus was present, with nonrelated rare spiking in the right temporal tip.

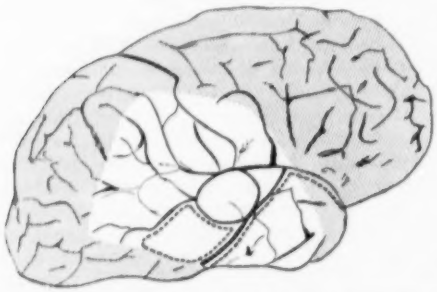

Fig. 3 (Case 3).—Sketch of the right hemisphere showing the temporal lobectomy and area of undercutting, outlined posteriorly by the interrupted line.

On July 31, 1952, with the patient under thiopental anesthesia, a bone flap was reflected in the left temporal region and the anterior 6 cm. of the left temporal lobe ablated. The specimen consisted of a piece of cerebral cortex weighing 30 gm. and measuring 6×5×2.5 cm. Histologically the tissue was reported as normal.

Following operation the patient was greatly confused; he declared his whole brain had been cut out and that he was going to sue the hospital for experimenting on him. His wound healed well, and he was discharged to his sister's care two weeks postoperatively.

When he arrived home, he had "no memory at all" remembered nothing of having been to Johns Hopkins or of any of the people there, even the patients he was confined with or events leading to his going there. Also, he could not remember the name of any employees whom he had worked with for the past five years, "which, of course, his sister said, was very alarming to his mother and myself. However, since then we have noticed a decided improvement in his memory, and, while it is far from normal, he can now remember most people and all about them at times and then the next day can't remember anything about them at all—in other words, his memory now seems to come and go from day to day except for the more important things and people. These he seems to be able to remember fairly good now."

Four months after his operation his brother wrote: "His memory, which was completely gone when he first returned home, showed remarkable recovery for the first 60 days and then seemed to just quit improving altogether, the result being that his memory at this writing is very poor. He remembers faces well enough but cannot remember names at all, and 30 minutes after a conversation on any subject he has forgotten conservatively 50% of the conversation and often has to be prompted to remember any of it at all, although with people he is very closely associated with, like his mother, he does much better, but yet is far from normal. As an example, he has asked me your name no less than a hundred times and quite often not over an hour apart, but it just does not seem to register with him."

The patient was seen again on May 19, 1955, almost three years after his operation. He stated that he had come here from Kansas City by bus, arriving a couple of days before. Then, after a few minutes he confessed that he was a bit confused and actually had been here a week. In fact, last Saturday he had gone to church, believing it was Sunday. He stated that his memory was considerably improved, although he still had difficulty in remembering the names of his associates.

New material, such as a paragraph of reading matter, was poorly recalled; in fact, the patient would not read more than a few lines because he couldn't remember it. A long explanation was given regarding the hospital policies on operation permits, about which the patient had paranoid ideas. He seemed to understand and be quite placated after the situation had been explained several times. But the next day he returned quite incensed that I had not talked to him about his operation permit! He was able to name common objects without difficulty, to give the months of the year, and to recite the Lord's Prayer without difficulty. However, when asked to define the meaning of words, he had trouble. He did not know the meaning of the word "dicker"; "elongate" was defined as "long gate." He was hesitant when asked what "jest" meant and finally stated that it was the same as "just." He was able to carry out simple mathematical problems involving addition and subtraction, although he made an occasional error in division. He could spell simple words without difficulty. When asked to repeat five numbers forward, he made no mistakes, but did make one error in repeating six numbers forward and seven numbers forward. Upon attempting to repeat four numbers backward, he transposed the figures and failed to repeat five numbers in reverse order.

He was rather garrulous and inclined to be outspoken and at times actually profane. In general, however, his conversation was logical and pertinent to the issue at hand.

He stated that he had had no attacks for the last few years and had been taking diphenylhydantoin morning and night and phensuximide (Milontin) twice a day.

An electroencephalogram was reported by Dr. Curtis Marshall as having a large amount of fast activity, presumably due to the medication which the patient had been taking.

This man obviously had a severe memory deficit, which persisted to some degree over three years. Granted that he probably was of border intelligence originally, his postoperative performance indicated gaps in higher mental function due to organic brain damage. He had a fair memory for remote events, but had both amnesic and organizational defects in mentation, as illustrated by his inability to recall and his confusion in time.

CASE 4.—A 40-year-old, right-handed housewife was admitted to the neurosurgical service because of severe headache. She was stated to have been in excellent health until approximately one week previously, when, shortly after sexual intercourse, she suddenly developed a severe headache, predominantly on the left side and behind the left eye.

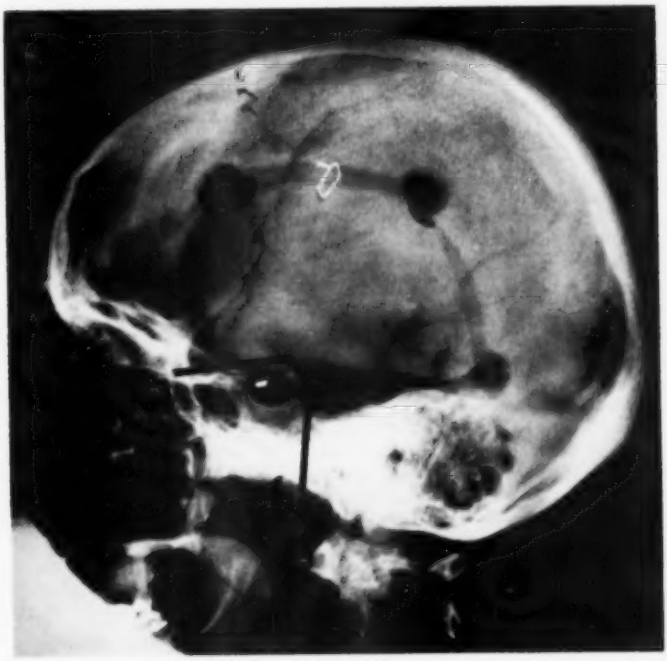

Fig. 4 (Case 4).—Lateral roentgenogram of the skull, with the presumed site of temporal lobectomy outlined by the black line. The clip on the neck of the aneurysm is seen along the sella turcica.

She became nauseated and vomited that evening. After a few days she was moved to The Johns Hopkins Hospital for further study. At the time of the patient's admission physical examination did not reveal any significant abnormality. On neurological examination there was slight ptosis of the left lid. No definite sensory disturbances could be demonstrated over the face. The remainder of the neurological examination was normal except for absence of the left ankle jerk, which had been known for some years. On lumbar puncture the initial pressure was 120 mm. of spinal fluid; the fluid was xanthochromic and contained some 2800 erythrocytes and 24 lymphocytes per cubic millimeter. Roentgenograms of the skull were said to be normal. An electroencephalogram carried out on July 27, 1955, was reported as normal by Dr. Curtis Marshall. On July 28 a left carotid angiogram was carried out, and an elongated aneurysm was found overlying the carotid siphon, presumably arising from the supraclinoid portion of the internal carotid artery. Immediately after the angiogram, the patient complained of diplopia and the following morning was found to have a complete third nerve paralysis on the left side. On July 30, with thiopental (Pentothal) anesthesia, the left carotid artery was exposed and a tape loosely applied around it. A horseshoe-shaped incision was then outlined in the left parietotemporal region and a four-hole bone flap turned down without difficulty, using the temporal muscle as a hinge. The dura mater was opened. The underlying cortex appeared normal. Through the second temporal convolution an incision was made and carried back for a distance of 5 cm., and the anterior part of the left temporal lobe was then removed in one piece. The medial portion of the temporal lobe was sucked away until one could see the margin of the tentorium and the fourth cranial nerve. Slightly medial and anterior to this nerve, a large, tortuous aneurysm ran along and compressed the oculomotor nerve until it entered the posterior aspect of the internal carotid artery just after its emergence from the cavernous sinus. At this point the neck of the vessel was practically the size of the internal carotid artery, but it appeared slightly more reddish and duskier than the gray internal carotid artery. An attempt was made to separate the third nerve from the aneurysm, but the adhesions were too firm. Accordingly, the neck of the aneurysm was then cleared, and a clip was applied to the neck just as it came from the internal carotid artery. The latter was not appreciably narrowed by this procedure. The aneurysm seemed to collapse upon the application of the clip. The dura mater was then closed and the bone flap replaced, being held with one tantalum wire suture.

The specimen, consisting of a grossly normal anterior temporal lobe, weighed 17 gm. and measured 4.2 cm. along the inferior border, 4 cm. along the superior border, and 3 cm. in width. Histological examination showed a considerable number of mononuclear cells in the subarachnoid space but otherwise no abnormalities.

The patient's convalescence was quite uneventful. Her husband noted within a day or so of operation that she had difficulty in remembering the names of her relatives. The patient had no difficulty in talking, but she continued to have trouble in naming people and occasionally would miss the name of an object. These memory disturbances gradually improved. On June 18, 1956, or 11 months after her operation, her mental status was investigated thoroughly. The patient complained that her memory was poor. Although she could remember all her household routine, she had difficulty in recalling the name of her golf partner of the previous day, or of neighbors or friends that she knew well. She usually recognized them but could not call them by name. Before her operation she read a great deal, but since she had done little reading of books or newspapers. She had gone only to one movie in a year "because her eyes hurt," and she did not like to look at television "because her mind wandered" and she lost the thread of the plot or show. She was unable to name the current President of the United States, although she knew earlier presidents.

She was able to draw accurately the floor plan of her home; but when asked to describe the route she had just taken to the examiner's office, she was unable to do so, although she made a few facetious guesses. Yet her hospital room of the previous year was accurately drawn.

Asked to recite "Mary Had a Little Lamb," she performed perfectly, and even sang a verse of "My Country 'Tis of Thee." She stated that some five or six months after operation she sat down and played the piano perfectly, which she had not done for months. Since then she had often played without difficulty, although she was having severe memory troubles at that time.

When given the adage, "The wise man learns from the experience of others; the average man from his own experiences; the fool never learns," with a nonspecific question regarding her health interposed between test phrase and response, she returned: "The wise man learns from others; the median doesn't accept what the other says. . . . I've forgotten." Yet she repeated six figures forward and backward.

On formal Wechler-Bellevue testing, she made a verbal score of 50 and a performance score of 43, giving a full scale I. Q. of 93. Only in the block design did she do poorly, seemingly being unable to comprehend the general patterns.

Her difficulties were demonstrated most clearly, however, when she was given a paragraph to read.

The first item concerned the results of an atomic bomb test, which she said she couldn't remember because she didn't like things that reminded her of bombs and war. She selected the theater as a subject in which she was interested and was given a paragraph describing the current metropolitan productions.

"They also vary considerably in merit. The best job is young actor T. C. Jones's female impersonations, especially of Tallulah. Short-haired Billie Hayes makes a lively ditty of 'I Could Love Him'; Virginia Martin, a lively ditty of 'Talent.' In 'La Ronde,' a foursome smoothly act out a liltish tune. Funniest spoof proves to be one more take-off on a big Ziegfield-era staircase number, with a showgirl rigged out like an entire orange grove, having a ghastly time on the stairs. There is fun in 'Steady, Edna,' which rags a British jungle film, in which an upper-class British domestic skit has a husband shouting, 'To hell with cricket,' and his wife replying coldly, 'Anyone who would say that would strike the Queen.'"

After reading through this paragraph, her recollection of the content was as follows: "There are a great many impersonations of famous people. They do an excellent job." She then copied in writing the paragraph and then wrote as the context:

"There were many impersonations on the stage. T. S. Elliot [Actually T. C. Jones] did an excellent job creating parts for stars. One star mimicked Tallulah Bankhead. Several others carried on very humorous roles."

She then wrote the paragraph to dictation and gave as her impression: "It gives four different shows. One is wonderful by T. C. Jones. Billy Martin is another. Then a girl in an orange grove. The other was 'To Hell with the Crickets.'"

She seemed aware of the deficiencies and cried, explaining that she couldn't help it.

Two days later she stated that the paragraph referred to "stars on the stage" and gave a number of examples, one of which concerned "something that was thrown."

This case, perhaps, illustrates the memory defects better than the others because the patient, being an educated teacher, is able to cooperate better in testing. It is apparent that she has no difficulties in pure motor memories—she does all mechanical and technical tasks, even to playing the piano or golf, as well as before operation. But ideational recall is so affected that she cannot follow a story on television or in a short paragraph. Her attention seemed to be adequate, and she was able to repeat both nonsense and meaningful material, provided that she did so while the "set" was still there, as evidenced by her ability to repeat numbers forward and backward. Yet, although the primary traces appear available, it would seem that the material is never or inadequately assimilated into mind.

Comment

Briefly, the mental changes resulting from some anterior temporal lobectomies have the following characteristics:

1. Superimposed upon a relatively intact intelligence, as measured by the formal I. Q. and normal personality, is a loss of memory for recent events with preservation of the ability to remember remote happenings. This may be so slight that the patient has no difficulty in carrying out his usual activities, or it may be so devastating that the patient cannot follow a drama or plot on television or radio.

2. Immediate recall is usually intact, for patients may be able to repeat nonsense syllables or series of numbers unless a minor diversion of attention is interposed between the giving of the test data and their repetition.

3. The memory impairment does not seem to affect the acquistion or retention of motor skills.

The observations upon memory loss following temporal lobectomy pose several problems. In the first place, are these phenomena due to focal lesions of the nervous system? In the second place, if they are the result of temporal lobe damage, why are they so infrequently seen? In the third place, why is ideational and not motor imagery implicated? And, finally, what anatomical and physiological mechanisms are involved in this amnesia?

It is generally considered that memory impairment is the result of diffuse brain involvement. Certainly, amnesia occurs in many conditions involving the brain diffusely—intoxications, head injuries, shock therapy, etc.—and occasionally temporarily after more localized damage to the brain.

However, even in the diffuse injuries severe memory disturbances persisting for years are not encountered unless associated with other evidence of mental impairment. Yet it might be argued that the first three patients had suffered diffuse brain damage as the result of their epileptic seizures. It is impossible to state whether or not such was the case, but at least functionally there was no evidence of such generalized injury. Neither the patient nor the relatives admitted memory alterations, before the temporal lobectomy, but all recognized the defects after operation. Nor was there evidence of general impairment of other mental functions, including intelligence, which commonly accompanies widespread cerebral alterations. And in the fourth case, it might be argued that the subarachnoid hemorrhage produced diffuse cortical changes. But against this is the fact that for a week after the bleeding the patient, although suffering severe headache, had no memory impairment. Finally, it might be propounded that the disturbances were due to minimal subclinical diffuse cortical damage plus the temporary lobectomy. This argument cannot be effectively answered, although the fact that memory disturbances are present in only a small proportion of such cases would militate against the assumption.

Memory disturbances occur in not more than 10% to 15% of temporal lobe resections and may be present after removal of the lobe of either the dominant or the nondominant hemisphere. An explanation for this rare occurrence of amnesia is propounded, based upon the view that the neuronal mechanism of memory is "probably duplicated in homologous areas of the two hemispheres." Milner and Penfield [6] have suggested that the opposite hippocampal zone must have been damaged by birth injury, so that removal of the epileptogenous temporal lobe left the person virtually deprived of the medial temporal structure on both sides. As evidence for this view, they point out that in their cases electroencephalographic abnormalities were present in the anterior temporal region contralateral to the lobectomy. In the present series, evidence of contralateral pathological alteration has not been demonstrable consistently by electroencephalograms or pneunoencephalograms. Moreover, several patients having bilateral temporal spikes have had unilateral lobectomies without their producing memory defects. Negative evidence, such as the above, although it does not confirm it, cannot invalidate the theory.

It might be argued that the so-called memory disturbances are really of an aphasic nature. Certainly, they are very prominent in all spheres where language is of paramount importance; but they do occur in nonlanguage situations, viz., the block arrangement of the Wechsler-Bellevue test (Case 4) and the difficulties in geographic and temporal orientation. It must be admitted that speech symbolism is affected, but the defect appears to involve aspects of mental functioning which are not ordinarily considered primarily related to language, and ordinary speech mechanisms do not seem to be implicated. Moreover, the fact that the disturbance might occur with lesions of either the dominant or the nondominant hemisphere would not support the hypothesis that the disturbance is basically aphasic in nature. True, aphasia disturbances of a different nature do occur after removal of the dominant temporal lobe.

Assuming that the temporal lobes are concerned with visual and auditory integration, another hypothesis might be proposed to account for the amnesia. It has been accepted since the time of Charcot that people may be divided on the basis of their imagery into acoustic-, kinesthetic-, and visual-minded groups.

Grey Walter [9] has modified this division slightly in order to correlate the classes with the characteristics of their electroencephalographic responses.

1. In persons tending to use auditory, kinesthetic, tactile, and visual imagery more or less equally in their imagery (about 67% of the population) the alpha rhythms dis-

appear and reappear as the eyes are opened and closed.

2. In persons tending to use auditory, kinesthetic, and tactile perceptions mainly or exclusively in their thinking (16%) the alpha rhythm persists when the eyes are opened.

3. In persons tending to use visual imagery almost entirely in their mentation (16%) the alpha rhythm is poorly developed and weakly, if at all, responsive to closing or opening the eyes.

This categorization is, perhaps, not quite as clearly defined as suggested by Grey Walter, but the generalization may be assumed to be valid.

If the integrating functions of the temporal lobe in the auditory and visual spheres were removed, the persons using auditory, kinesthetic, and tactile perceptions would have minimal disability and those employing all forms of imagery equally well would likewise have no apparent deficit. But those relying upon visual imagery, about 16% of the population, would be profoundly disturbed.

Might the patients, amnesic following unilateral temporal lobectomy, belong to this third group? This interesting question cannot be conclusively answered on the basis either of preliminary psychological testing or of electroencephalograms in the present series. Three of five patients having memory disturbances after temporal lobectomy (the four cases reported here and a fifth with a temporal-lobe tumor) had poor alpha rhythms; unfortunately, the preoperative response to eye closure is not recorded in these cases; in the other two cases the alpha waves were augmented upon closing the lids. This hypothesis must be tested in a larger series of cases before any conclusion can be drawn.

The selective impairment of ideational memory with sparing of kinesthetic imagery would seem to indicate that the basic physiological disturbance was probably localized, and not a general effect upon all neuronal retention. The localization of visual and auditory integration in the temporal (and perhaps the occipital) lobe would allow a circumscribed disturbance to impair these faculties, leaving unaffected the motor and somatosensory systems, which are located in frontal and parietal lobes.

The part of the temporal lobe responsible for the memory loss in these cases cannot be stated with certainty on the basis of this material. From the reports of Grünthal,[5] Glees and Griffith,[4] and Scoville,[8] it would appear to be the medial temporal structures. Milner and Penfield[6] assume without direct evidence that hippocampal damage is essential to the syndrome, since the few cases of bilateral amygdaloidectomy and uncotomy reported have not had such memory disturbances. Although unilateral, lateral, and anterior temporal lobectomies are said not to give rise to a memory loss, it may be that a combination of temporal cortex, amygdala, and hippocampus is necessary to produce the syndrome. It seems unlikely that the afferent and efferent temporal connections carried by the fornix are responsible, for neurosurgeons have cut the fornix in removing third-ventricle tumors and Bengochea et al.[2] have sectioned it for the relief of epilepsy without producing such memory defects. Similarly, the interhemispheric connections seem unlikely, for agenesis of the corpus callosum or section of the corpus callosum does not produce this syndrome.

Assuming that the hippocampus damage is critical, does injury to these structures destroy pathways or neuronal constellations in which are stored memory traces? This is unlikely, since the memories are not gone but merely cannot be called up to consciousness; the patient is aware of the loss and recognizes the correct memory. Moreover, it would seem improbable that so many memories could be stored in one or two gyri. On the contrary, it seems more likely that in the hippocampal gyri is a mechanism by which memories stored in other areas are allowed to "jell," or fix, so that they are accessible at later times. Whether a lesion of this area eliminates this jelling process

by destroying a positive "memory-fixing" system or by releasing subcortical or cortical structures to augmented activity, thus preventing them from functioning normally in memory processes, cannot be stated. That temporal lobectomy has such a general effect upon neuronal activity is indicated by the depression of the ipsilateral alpha rhythm after the temporal lobectomy. Further investigation is necessary to answer these questions.

Summary

Four cases of temporal lobectomy are presented to illustrate the type of memory defect which may occasionally follow such lesions.

The amnesia is characterized by severe impairment of recent and little involvement of remote memory.

The explanation of the rarity of this complication is discussed.

The anatomical basis would seem to be local cortical, possibly hippocampal, damage rather than interruption of afferent or efferent tracts from the medial temporal structures.

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Diffuse Meningiomatosis, Arachnoidal Fibrosis, and Syringomyelia

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The relation of three apparently separate entities is considered in the unusual case reported here. The sequence of events is believed to be as follows: A diffuse spinal meningiomatosis plus occasional meningioma formation and repeated laminectomies caused a widespread fibrosis of the arachnoid, and the latter process resulted in formation of cavities in the spinal cord.

Report of a Case

Paraplegia and removal of meningioma; later recurrence of meningiomas. "Arachnoiditis" found at fourth and fifth laminectomies. Postmortem findings of many meningiomatous foci, arachnoidal fibrosis, and intramedullary spinal cavities.

In 1939, at 28 years of age, this woman first complained of pain in the thoracic region, weakness of the legs, numbness below the nipple line, and loss of sphincter control. She was admitted to a hospital, where examination revealed a spastic paraplegia, hypoactive reflexes, a bilateral Babinski sign, and impairment of sensation up to the second thoracic dermatome. Laminectomy was performed from the seventh cervical to the second thoracic vertebra, and a meningioma was removed. The dura was opened, and the spinal cord had a normal appearance. Recovery was complete, and she was walking well in January, 1940, when she was discharged from the hospital. In 1945 she was readmitted for similar complaints. Laminectomy, using the original incision, disclosed a recurrent intradural meningioma, extending from the second to the fourth thoracic vertebra. The spinal cord before removal of the tumor was displaced to the left and angulated. The tumor measured 2.5×1.0×1.0 cm. and was removed, with wide excision of the surrounding dura. A cellophane membrane was placed at the site of the removed dura. A third operation was performed in February, 1948, using the same incision, and again a meningioma was found at the second and third thoracic levels. The patient was improved when discharged from the hospital, but had residual spasticity and weakness of the lower extremities. She was otherwise well until October, 1949, when she noticed the return of pain in the shoulders and weakness in the right upper extremity, as well as numbness along the ulnar aspect of the left forearm. A fourth laminectomy, extending from the fourth to the seventh cervical vertebra, disclosed dense adhesions in the arachnoid and dura. The spinal cord appeared normal, but was softer than usual at the lower end of the incision. A needle was inserted without obtaining fluid. The postoperative diagnosis was "adhesive arachnoiditis with degenerative changes in the spinal cord." The patient was discharged from the hospital in October, 1950, with good power in the lower extremities, hyperactive reflexes, sustained ankle clonus, and a bilateral Babinski sign. In April, 1951, she was admitted to Montefiore Hospital because of progression of symptoms.

Examination disclosed weakness of all extremities and severe atrophy of the muscles of both arms. The leg muscles were not atrophic. The biceps and triceps reflexes were absent on the right, and clonus was noted in the right ankle. Pain sensation was absent in a band from the first to the fourth thoracic dermatome on the right, and the first to the sixth thoracic segment on the left. Touch sensation was not altered. Sense of vibration was absent below the nipple line. By January, 1952, the band of analgesia extended bilaterally from the 1st to the 10th thoracic dermatome.

The routine blood count was normal, as were the blood sugar and urea nitrogen. The cerebrospinal fluid protein on different occasions ranged from 195 to 236 mg. per 100 cc. Roentgenograms of the chest revealed partly calcified nodular densities in the upper third of both lung fields. Roentgenograms of the vertebral column showed residuals of the cervicodorsal laminectomies.

The patient was treated conservatively until July, 1953, when motor and sensory impairment in-

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creased. A myelogram revealed a block at the ninth thoracic vertebra. Laminectomy was then performed from the 8th to the 10th thoracic vertebra and disclosed thick connective tissue adherent to the spinal cord. At the lower edge of the wound, a calcified plaque was found on the dorsal surface of the cord with dilated cephalad veins. The plaque was easily removed. A slit in the dorsum of the spinal cord revealed an intramedullary cavity. A polyethylene tube was inserted in an effort to drain the contents of the cavity into the subarachnoid space. The postoperative diagnosis was "intramedullary cyst and arachnoiditis with calcification." Postoperatively the condition of the patient worsened, and she became completely quadriplegic with diffuse muscular atrophy.

In November, 1953, she went into shock, with no recordable blood pressure, and with tachycardia and abdominal pain and distention. Bowel sounds were not heard, and tenderness in the right lower quadrant was noted. Therapy consisted of antibiotics, gastric intubation, and intravenous fluids. A barium enema was performed to rule out an intrinsic lesion of the colon, but this was not found. The patient then improved on therapy which included the use of parasympatheticomimetic and vasoconstrictor drugs. At the beginning of December she again went into shock and had a gallop rhythm. She continued to do poorly, and her temperature rose to 105 F. A blood culture revealed Escherichia coli. The patient died at the beginning of January, 1954.

Necropsy.—The general autopsy revealed purulent peritonitis and abscesses in the heart and kidneys. Postmortem blood cultures contained E. coli. The cerebral dura and brain were normal. In the spinal cord, an ascending demyelination was noted in the uppermost cervical levels. From the lower portion of the cervical region to the cauda equina, the spinal cord was bound by intense adhesions, which were cut with difficulty (Fig. 1). When sectioned, the spinal cord had the appearance of a collapsed tube, measuring only a few millimeters in anteroposterior diameter. A polyethylene tube, 13 cm. in length, lay adjacent to the spinal cord, with the upper end of the tube lying within adherent leptomeninges rather than in the spinal cord. The lower end of the tube was enmeshed in dense adhesions between pachy- and leptomeninges in the lumbar region. The cut surfaces of the spinal cord were discolored yellow, and two separate cavities were seen on either side of the midline in the cervical region. The cavities were collapsed in the postmortem specimen and therefore resembled slits in the mediolateral plane. Similar single or multiple cavities were seen at all levels down to the sacral region, as well as massive adhesions between dura, leptomeninges, and spinal cord. The cavities lay predominantly in the posterior half of the spinal cord.

Microscopic Findings.—The dura, for the most part, was normal in appearance. The leptomeninges, however, had undergone a widespread alteration. Loose and dense connective tissue lay between dura and spinal cord, often two or three times the thickness of the normal dura. Few inflammatory cells were seen in the thick arachnoidal membranes. Numerous meningiomatous cells lay within the connective tissue. These cells were seen singly or in clusters, often forming whorls and accompanied by psammoma bodies. Meningeal-cell clusters were encountered on the epidural as well as the subdural surface (Fig. 2). They surrounded and penetrated the nerve roots in epineural and perineural tissues (Fig. 3*A* and *B*). Connective tissue proliferation was also evident in these locations.

Fig. 1.—Photograph of the spinal cord with the dura mater opened. The polyethylene tube (cut post mortem) lies in dense adhesions. The spinal cord is flattened. Cross sections at three levels are shown above, with two cavities seen in the cervical region (upper right).

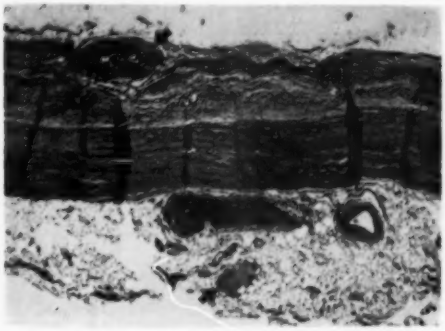

Fig. 2.—Photomicrograph of the dura with arachnoidal fibrosis above. The upper arrow indicates a meningiomatous whorl in the thick arachnoid; the lower arrow shows a similar cell mass in the epidural fatty tissue. The dark vertical bands are artifacts. Hematoxylin-eosin preparation; reduced to 80% of mag. × 18.

The fibrotic process extended into the anterior median fissure, surrounded the anterior spinal artery and vein, and was seen around most of the small, deep blood vessels. The pial vessels were thicker than normal in some places, but more frequently were only slightly altered. The microscopic picture was similar, with moderate differences in degree, from the upper cervical to and including the sacral levels.

The cavities in the spinal cord were of two varieties (Figs. 4 and 5). One type had irregular walls and contained pink-staining, protein-rich fluid and occasional macrophages; the other kind of syrinx was smooth-walled and lined by condensed glial fibers.

Microscopic Diagnosis.—Spinal arachnoidal fibrosis secondary to diffuse meningiomatosis and repeated laminectomies; infarcts in spinal cord; syringomyelia.

Comment.—The clinical evidence strongly supports the concept that this problem began as an uncomplicated removal of a spinal meningioma, with visualization of a normal spinal cord. A total of five laminectomies was performed and the resulting blood and operative trauma contributed to "arachnoiditis"; but connective tissue proliferation was noted far beyond the explored fields, and even around epidural portions of nerve roots. The steadily progressive nature of adhesive arachnoiditis has often been puzzling, but the finding of epi- and subdural dissemination of microscopic meningiomas provides an adequate explanation in this case. On clinical grounds, also, it may be suspected that intramedullary cavitation was present in the thoracic region in 1951, because of the "suspended," or band-like, analgesia. It is not possible to date the onset of the syrinx more accurately. Progression of the cavitation, however, is shown clearly by extension

Fig. 3.—*A*, photomicrograph of epidural portion of thoracic spinal nerve. Epineural and perineural tissue is thickened, and a few psammoma bodies are seen within a nerve fascicle. Hematoxylin-eosin preparation; reduced to 80% of mag. × 10.

B, Higher-power view of portion of nerve shown in *A*. Meningocytes form sheets and whorls. In addition, psammoma bodies and proliferated connective tissue are seen. Hematoxylin-eosin preparation; reduced to 80% of mag. × 95.

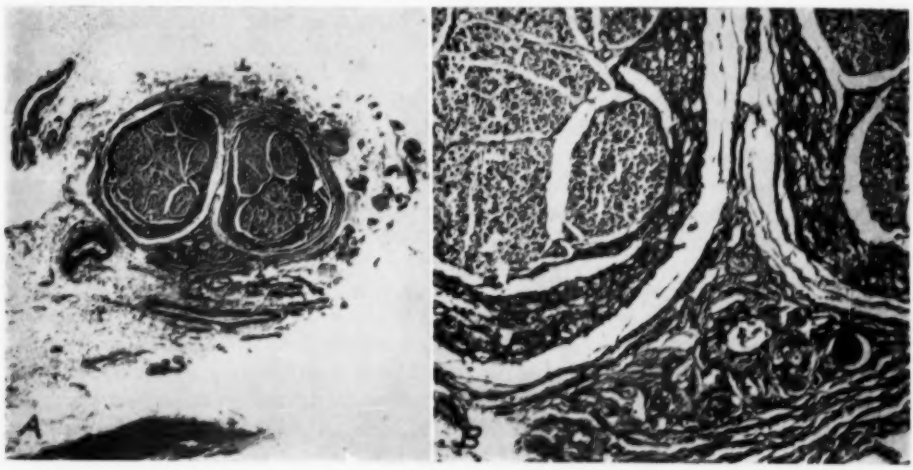

Fig. 4.—Photomicrograph of cervical region of spinal cord. Two smooth-walled cavities are present, as well as an irregular zone of infarction in the posterior column. Hematoxylin-eosin preparation; reduced to ⅔ of mag. × 5.5.

of the analgesic band noted in January, 1952.

The meningioma removed at the first laminectomy (reviewed through the courtesy of Dr. Abner Wolf) contained typical meningocytes and psammoma bodies, as well as a large fibrous tissue component, and was comparable histologically to the disseminated small meningiomas seen at necropsy. The fibrous tissue could be considered as a part of the diffuse meningioma, but there is no morphologic distinction from non-neoplastic connective tissue. It is probably correct to view the widespread fibrosis as a reaction within the meninges to diffuse meningiomatosis and the repeated trauma of laminectomies.

The findings within the spinal cord offer evidence of a pathogenesis of syringomyelia. It is inferred that arachnoidal adhesions interfere with blood supply, leading to infarction and exudation of plasma. The microscopic picture was of slowly progressive infarction leading to cavitation of the spinal cord. This slow process caused a mild macrophagic response with later disappearance of these cells. The cavity thus formed was walled off by glial cell processes.

General Considerations

Meningiomatosis and Meningiomas.—The term meningiomatosis has been applied to cases with multiple meningiomas,[1] as well as to widespread sheets of neoplasm covering the meninges. To distinguish the two entities, "diffuse meningiomatosis," or

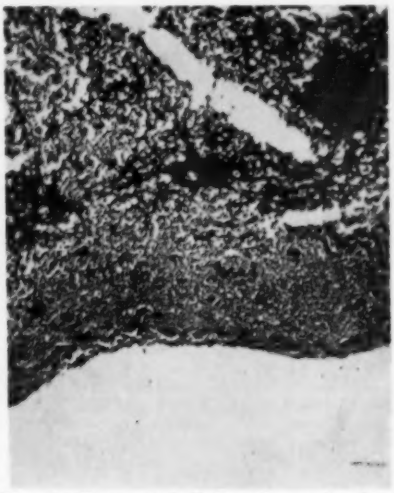

Fig. 5.—The smooth lining of a syrinx is seen below. The more recent cavitation is shown above with frayed myelin partially infiltrated by a homogeneous, protein-rich fluid, but little cellular exudate. 88% of mag. × 80.

"meningeal meningiomatosis," has been applied to the latter process. Weinberger[2] discussed this process and concluded that diffuse tumors are best explained on an embryonic basis by meningeal rests attempting to reproduce meningeal structures. He stated that he failed to find evidence of extension of the tumor by implantation or seeding, but the case reported here shows extradural tumor, which is difficult to explain embryologically. Black and Kernohan[3] reviewed many of these tumors and doubted the role of rests in the process. They suggested that tumors might arise in large areas of arachnoid without indicating an embryonic origin. The total number of reported cases of diffuse meningiomatosis is difficult to calculate, because many cases have been labeled as sarcomas or other diffuse neoplasms, and it is often difficult to decide whether these diagnoses are correct. Cavitation in the spinal cord was not found in any of the reported cases with the exception of the single instance of Black and Kernohan,[3] in which they described recent infarction of the thoracic portion of the spinal cord.

Single meningiomas of the commoner, discrete variety have been described in as-

sociation with syringomyelia.[4-8] These reports were reviewed by Poser.[9] Conclusions drawn from grouping such cases must be viewed with caution, as is shown when this series is analyzed in detail. In the first case [4] a meningioma was found in the cervical region with a cervicothoracic syrinx. Although tumor and cavity were not immediately contiguous, the probable explanation of cavitation is the circulatory effects of compression of blood vessels. This has been discussed in detail in another publication.[10] In the second case [5] a meningioma was seen at the level of the first thoracic spinal cord segment. The syrinx is described as "a not very severe split" and was seen at all levels of the available specimen, but the total extent of the specimen is not described. The illustration of the spinal cord at the level of the neoplasm reveals a dilated central canal, and the described syringomyelia is not shown at any other level. The case is further complicated by a severe spondylitis deformans. It is probable that the split was a hydromyelia (enlarged central canal) rather than cavitation within the substance of the spinal cord. In the third case [6] a meningioma was found lying behind the medulla and the upper part of the spinal cord down to the fourth cervical nerve. A syrinx at sixth and seventh cervical levels was directly associated with massive arachnoidal fibrosis and cyst and bone formation from the sixth to eighth cervical segment. In this latter case, similar in some ways to the case reported here, it is difficult to relate the meningioma and the syrinx, and it is likely that the arachnoidal fibrosis is the better-related cause of cavitation. It does not seem likely that the fibrosis was caused by the distant meningioma. In the fourth case [7] the meningioma was in the fourth ventricle and the cavity in the medulla oblongata, a direct association, and therefore similar to the first case. In the fifth case [8] a man had a cerebral parasagittal meningioma and a typical cervicothoracic syrinx with minimal extension into the medulla. This case, then, represents a coincidence of two dissimilar lesions, and cannot justifiably be used to indicate the direct relation between syringomyelia and neoplasia.

Arachnoiditis.—Chronic adhesive arachnoiditis has been described under a variety of names, including serous spinal meningitis, chronic spinal meningitis, chronic spinal arachnoiditis, and arachnoid cysts.[11] Arachnoidal fibrosis is a better term, because inflammation may be lacking histologically, and there is often no evidence of inflammatory agents as etiologic factors, whereas the common feature is connective tissue proliferation. "Arachnoiditis" has achieved such widespread use that it cannot easily be changed. Arachnoiditis may be focal or diffuse, but this discussion deals chiefly with the diffuse type. The causes of diffuse chronic adhesive arachnoiditis include infections within the leptomeninges; trauma to the spine, or spinal cord; subarachnoid bleeding or introduction of other intrathecal foreign material, and, as indicated in this report, diffuse involvement of the leptomeninges by meningioma and, presumably, other neoplasms. The origin may not be determinable in some cases.

It is often stated that systemic diseases, such as gonorrhea or influenza, may cause arachnoiditis, but it is doubtful whether this occurs unless associated with meningitis. Horsley [12] obtained a history of preexisting gonorrhea in several of his patients and attributed the subsequent "chronic spinal meningitis" to this agent, but without direct evidence, as he was well aware. Subsequent cases due to gonorrhea have not been reported.

There are reports that diffuse adhesive arachnoiditis may be the result of intrinsic disease of the spinal cord (e.g., multiple sclerosis or syringomyelia). This is difficult to understand if the disorder is confined to the substance of the spinal cord. Plaques of multiple sclerosis may reach the surface and produce a few small adhesive bands, but a large experience with cases of this disorder at necropsy has shown that arachnoiditis is only an occasional and minor

finding.[13] This is equally true of syringomyelia and other purely intramedullary disorders. Cases have been described[14] in which syringomyelia was associated with major forms of arachnoiditis, but the arachnoiditis may have been responsible for the syringomyelia rather than the reverse.

Removal of a spinal neoplasm may result in focal adhesions. Indeed, simple opening of the dura with manipulation of the arachnoid may produce scarring.[15] Introduction of blood at the time of laminectomy may result in more widespread adhesions. Evidence of progressive alteration of spinal cord function may occur after removal of a meningioma, and the problem will then be raised how to differentiate recurrence of meningioma from arachnoiditis.[16] This is difficult clinically, and reexploration may be necessary. If only arachnoiditis is found, another question is the mechanism of progression of the fibrosing process. A single trauma should not result in a propagating fibrotic reaction, although increasing pressure be a fluid-filled cyst may on occasion by the cause of progressive cord dysfunction. Davidoff et al.[16] suggested that diffuse meningiomatosis might be one of the irritating factors responsible for the continuance of arachnoidal fibrosis. The present case offers evidence for this concept. Diffuse meningiomatosis should then be added to the list of causes of diffuse adhesive archnoiditis.

Can arachnoiditis cause diffuse meningiomatosis? There seems no doubt that irritation by many agents may cause proliferation of preexisting foci of meningeal cells, as well as connective tissue proliferation, resulting in scar tissue. But such proliferation is in immediate and obvious relation to the irritative factor and does not extend extradurally, or to regions of the meninges not affected by arachnoiditis. Whether this proliferation can result in formation of neoplasms is not known at present. In the case reported here, the evidence indicates that the neoplasm preceded the arachnoidal fibrosis.

Syringomyelia.—Syringomyelia in the sense of cavitation in the spinal cord has multiple causes. Extramedullary compression or arachnoiditis; intramedullary neoplasm; spinal cord trauma,' softening, inflammation, or maldevelopment—all may result in cavity formation. The first case of adhesive arachnoiditis and syringomyelia was described by Schwarz in 1897[17] under the name of "syphilitic myelomeningitis." The evidence for syphilis in this case is not certain. Nevertheless, Schwarz presented a detailed pathologic description and noticed the presence of cavities in the cord. Arachnoiditis in association with syringomyelia has been reported in at least 11 other verified cases.[6,18-25]

Review of these cases reveals that the patients ranged in age at onset from 3 to 50 years. Eight of the eleven patients were of the male sex. The disease lasted from 4 months to 11 years, but usually 1 to 2 years. The most frequent causative factor was trauma, but in some cases there was no known cause. In Nelson's case,[23] thrombocytopenic purpura and convulsions may have caused repeated bouts of meningeal bleeding, with subsequent fibrosis. Kramer[25] reported a case in which intrathecal medication was responsible. Aside from the early case of Schwarz,[17] syphilis was not implicated as a causative factor, and it is questionable in his case. The usual clinical picture was a progressive spastic paraplegia, and the presence of intramedullary cavitation was not often suspected clinically. At laminectomy or necropsy, the arachnoid was always observed to be thick, and the dura was often similarly affected. The arachnoid frequently contained cysts. In general, there was correspondence between the extent of arachnoidal fibrosis and the cavity formation in the spinal cord. Cavities were often limited to the cervical or thoracic regions, but occasionally were encountered throughout the extent of the spinal cord. The syrinxes were single or multiple, individual cases often revealing different patterns at various levels. The cavities tended to occur in the

posterior half of the spinal cord, often within the limits of the posterior horns.

In the case of Harbitz and Lossius,[6] a large meningioma was encountered behind the medulla oblongata and the upper part of the spinal leptomeninges. This is similar to the present case, although diffuse meningiomatosis was not found. Lubin[22] described "in several places connective tissue fibers . . . arranged in tumors resembling meningiomas." The remainder of the reported cases did not reveal meningeal or other neoplasms.

The association of syringomyelia with spinal intramedullary neoplasms, and to a less degree with extramedullary neoplasms, has been noted by Poser[9] in a review of 234 cases. There are inherent dangers in uncritical compilations of cases from the literature. Many reports are written from a limited point of view, and usually are not designed for studies of incidence. As an example, in my review of eight cases of syringomyelia,[26] I specifically excluded all instances with associated spinal neoplasms. Such a series, therefore, should not be included in a review of "incidence of intramedullary tumors found in autopsied cases of syringomyelia." Whether a case is considered one of "syringomyelia with neoplasm" or of "neoplasm with syringomyelia" will depend often on the interests and orientation of the observer rather than on knowledge of which came first or was causative.

Factors of selection may distort statistical complications. The choice of a group of patients with a chronic disorder may result in a larger number of associated neoplasms than in a series of patients with a more acute illness. This may be illustrated by our report on multiple sclerosis,[13] with 41 complete necropsies and 10 instances (24%) of coexisting neoplasms. By contrast, our amyotrophic lateral sclerosis[27] series, of 46 cases, contained only 1 instance of cancer (2%). This was true despite the fact that the average age at death was 51 years in the latter group and was only 45 years in the multiple sclerosis series. There is at present no verified explanation for the high incidence of associated neoplasms in multiple sclerosis necropsies, but an etiologic relationship has no support in available data.

Other selective factors may confound the statistician. Syringomyelia is rare clinically, and necropsy cases are seldom encountered except in large centers and specialized institutions. The syringomyelic patient is often excluded, because few hospitals take care of the chronically ill. The more spectacular course of many patients with intramedullary tumor is likely to lead to admission to the hospital. In addition, diagnostic or complicated problems will more frequently result in necropsy, because permission will be more eagerly sought, whereas the uncomplicated problem will be dealt with more perfunctorily.

Reports in the literature, furthermore, are a poor source of information about frequence, because common conditions often are not reported, as few authors desire (or are allowed) to add more cases of an already well-described disease. But the unusual and bizarre cases do enter the literature, as exemplified by this paper. Instances of multiple lesions also fall into the reportable category.

Some of these factors may cancel each other, but they represent variables of unknown magnitude. It is clear that there may be an association of intramedullary neoplasm and syringomyelia (or the reverse), but the figure is small and not exactly known. It is also clear that the majority of cases of syringomyelia are not associated with neoplasms, and the majority of intramedullary tumors do not coexist with syringomyelia.

Syringomyelia and Recklinghausen's Disease (Neurofibromatosis).—The association of multiple meningiomas and neurofibromatosis has been noted by Hosoi,[28] who reviewed 22 cases of multiple meningiomas and found 5 with generalized neurofibromatosis and another 5 with uni- or bilateral acoustic nerve tumor without multiple neurofibromas. Multiple meningiomas have been viewed as a special variant of Recklinghausen's disease,[29] but this has not been proved. Syringomyelia may occur in patients

with neurofibromatosis,[30] but the frequence is not known. This association has been used to suggest that syringomyelia is a part of the complex of Recklinghausen's disease.[9] It should be emphasized that association of disease processes is not adequate proof of a causal relation or of a common pathogenesis. The absence of neural tumors and other stigmata of Recklinghausen's disease of nerves, clinically and at necropsy, prevents the applicability of this diagnosis in the case reported here, despite the generalized and recurrent formation of meningiomas. Furthermore, the numerous other instances of spinal arachnoiditis without tumor make Recklinghausen's disease an unlikely cause of cavitation in these cases.

Pathogenesis of Syringomyelia.—The mechanisms suggested whereby arachnoiditis may cause syringomyelia are as follows:

1. Interference with arterial and/or venous blood supply
2. Direct compression of the spinal cord
3. Fixation of the spinal cord by adhesive bands and progressive trauma from repetition of respiratory excursions and movements of the spine[11]

If thrombosed arteries or veins are found, no doubt will exist as to their role in the process. The vascular factor is less certain when patent (even though narrowed) lumens are found. Blood vessels surrounded by dense connective tissue certainly are less efficient, but it is difficult to judge the degree of functional incapacity at the postmortem examination by gross or histologic methods. It is of interest that cavitation in the reported cases of arachnoiditis was seldom in the specific distribution of the anterior or posterior spinal arteries. Cavities were occasionally disseminated, but most frequently were in the anterior part of the posterior column. This most commonly affected region contains the terminal branches of both major arteries. This suggests insufficiency of the small vessels, and connective tissue proliferation surrounding both large and small vessels may be a contributing factor.

If blood vessel insufficiency is an important mechanism, it is more logical to implicate the easily compressed veins than the arteries. Despite this, most authors speak of arterial compression. Inasmuch as the venous supply parallels the arterial supply, the resulting lesion would be in a similar distribution. This was emphasized in the report of Chung,[31] in which syphilitic thrombosis of veins in one case, and of arteries in another, resulted in a similar anatomic lesion.

The role of direct compression of the spinal cord by the sclerotic meninges is difficult to judge. In none of the reported cases was the spinal cord physically distorted. Stookey's[11] concept of repeated trauma is better applicable to focal arachnoiditis with movement of the spinal cord above and below the point of fixation than to diffuse arachnoiditis.

Arachnoiditis may be created experimentally and result in cavitation in the spinal cord.[32] This adds further support to the concept that arachnoiditis may cause syringmyelia. It is of interest that the first evidence of cavitation with induced arachnoiditis is in the ventral portion of the dorsal columns, just behind the central canal. This locus is also the first site of cavitation when the anterior spinal artery is ligated[33] or thrombosed. In primary syringomyelia, the region dorsal to the central canal is also commonly involved, but exceptions are sometimes found.[26]

Summary

A patient suffered from multiple meningiomas of the spinal cord and later from an arachnoidal fibrosis and syringomyelia. At necropsy, multiple epi- and subdural microscopic foci of meningiomas were found. It is suggested that these tumors (and the repeated trauma of laminectomies) caused proliferation of connective tissue in the leptomeninges and led to infarction of the cord with subsequent syrinx formation. The relations of diffuse meningiomatosis, arachnoidal fibrosis, and syringomyelia and their causation are discussed. Diffuse meningiomatosis is added to the list of causes of diffuse adhesive arachnoiditis, and in some cases may account for the progressive nature of the latter process.

Ben D. Morton Jr. took the photomicrographs.

The Bowman Gray School of Medicine of Wake Forest College.

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Studies on Effect of the Injection of Alumina (Aluminum Oxide) Cream into the Basal Ganglia

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Introduction

Investigation of the role of subcortical structures in epilepsy has been pursued by various methods. Electrical stimulation has been fruitful but has certain obvious limitations. Chemical excitation has produced only occasional significant results. Recently we have reported[3,4] on the results obtained by the use of penicillin injected into subcortical structures. Though the seizures obtained were dramatic, the opportunity of studying the character of the attacks was somewhat limited by their transient nature. To obtain animals with a more chronic form of epilepsy, we undertook a series of subcortical injections with a standardized preparation of alumina (aluminum oxide) cream,[2] known to yield consistent results when placed in the motor cortex in sufficient quantity (more than 0.1 cc.).

Method

Sixteen immature monkeys (two Macaca mulatta and fourteen Cebus monkeys), weighing between 1 and 3 kg. were used. Control electroencephalograms were obtained prior to the injection of alumina cream.

The injections into various subcortical structures were performed by freehand technique through previously prepared frontal trephinations, or small openings in the skull made with a Turkel bone marrow trephine. For the injection, a tuberculin syringe and 22-gauge lumbar puncture needle were employed, considerable care being taken to avoid cortical contamination or reflux along the needle tract. Eighteen injections of 0.2-0.25 cc. of the standarized colloidal suspension of alumina cream (containing 18-22 mg. of alumina per cubic centimeter) were made, two in each macaque at three-month intervals on opposite sides, and one in each Cebus.

The animals were then observed almost daily by trained personnel and periodically provoked to highly excited states by vigorous physical exercise. The observation period, except in one animal that died three days after injection, varied from 5 weeks to 14 months, the average being 7 months. During this time, serial scalp recordings employing eight solder electrodes placed in standard positions (4) over the frontal, temporal, central, and occipital cortex bilaterally were made at varying intervals on a Model III Grass eight-channel electroencephalograph. During each recording, the animals were stimulated with known, usually subconvulsive doses of pentylenetetrazol U. S. P. (Metrazol). At the end of the observation period, seven of the animals were killed in acute experiments, in which multiple subcortical recordings were performed. After the animals were killed, the brains were serially sectioned and stained for cells (Nissl) and myelin (Smith-Quigley) in order to determine the exact site of the injection and stimulation histologically. Photomicrographs of representative sections were then prepared.

The lesions produced were located as follows: thalamus, 3; amygdala complex, 6; globus pallidus and putamen, 3; putamen and amygdala, 1; nucleus basalis, 1; pons and mesencephalon, 1. The location of the injection sites was not confirmed histologically in three instances (C-4, C-5, and C-13). For the most part the character of the lesions was similar to that described by Kopeloff et al.,[5] consisting of a delicate connective tissue capsule containing masses of compound granular cells engorged with alumina, interlaced by delicate capillaries and without discernible neural elements. Two of the lesions (M-61, left thalamus, and C-1, right mesencephalon and pons) were cystic. Representative photomicrographs of the lesions at the point of their maximum extent are illustrated in Figure 1.

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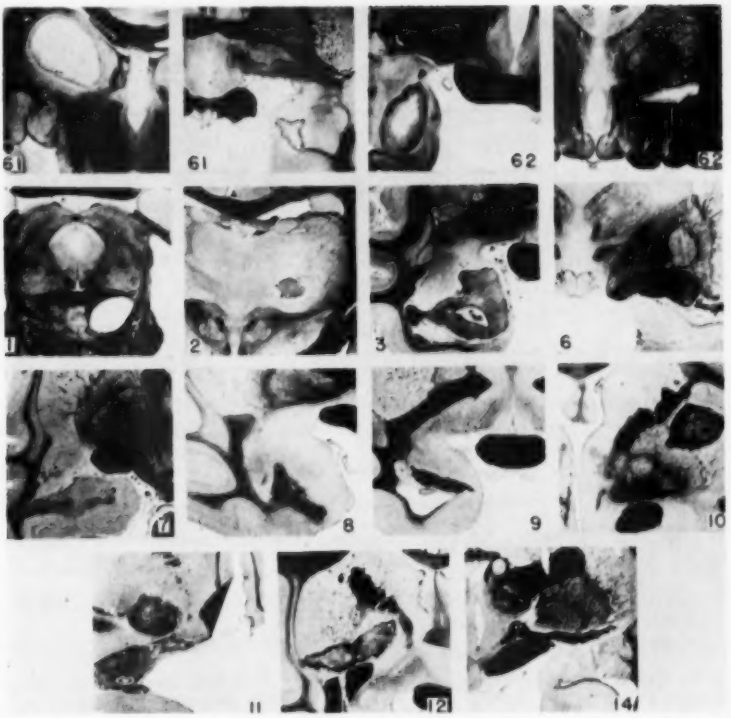

Fig. 1.—Photomicrographs of representative sections of the lesions at the point of their maximum extent produced by the subcortical injection of alumina cream. Smith-Quigley stain; reduced approximately 2/3 from mag. × 6.

Results

1. None of the animals developed spontaneous clinical seizures during the observation period.

2. Alterations in the chronic electroencephalographic pattern were noted in the animals having thalamic and striatal lesions but not in the monkeys with injections in the amygdala.

Of the seven animals having verified amygdala injections, four had dominant alpha frequencies and three dominant beta frequencies in their control records. In only one of these animals was there a significant change in frequency or amplitude of the spontaneous activity or an alteration in the paroxysmal bursts of biparietal sharp waves. In this animal (M-61) there were transient spiking in the ipsilateral central lead and a generalized depression of alpha activity.

All three animals having intrathalamic injections had preliminary alpha dominant frequencies in their electroencephalograms. Following injection, two of the animals had persistent beta rhythms and fewer biparietal bursts. The third animal, in which the lesion damaged the *centre médian*, had generalized augmented alpha activity in terms of both voltage and percentage occurrence in time, and larger biparietal spikes on the side of the lesion. A fourth animal (C-6), having an injection at the base of the thalamus in the vicinity of the subthalamic nucleus, had no alteration in the spontaneous electrical activity.

Three animals having striatal lesions had dominant alpha frequencies in the electroencephalograms, and one, beta frequencies. In all four monkeys there was increased amplitude of the biparietal bursts on the side

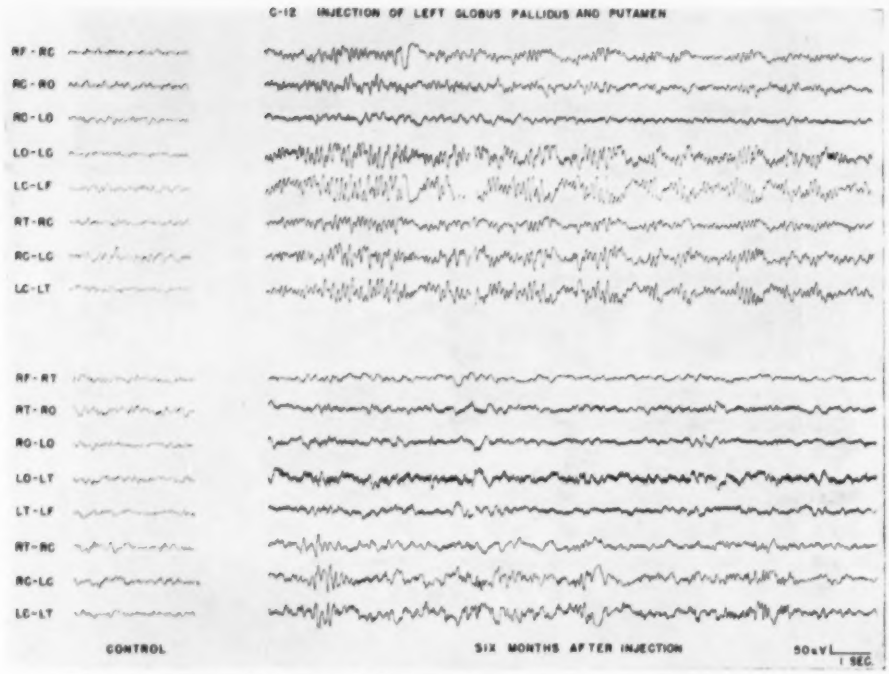

Fig. 2.—Electroencephalogram of Monkey C-12. At the left a sample of the preinjection control record, and at the right a trace taken six months after the injection of 0.2 cc. of alumina cream in the left globus pallidus and putamen. In the latter, note bursts and runs of high-voltage (100μv) sharp waves, consistently reversing on the left central lead.

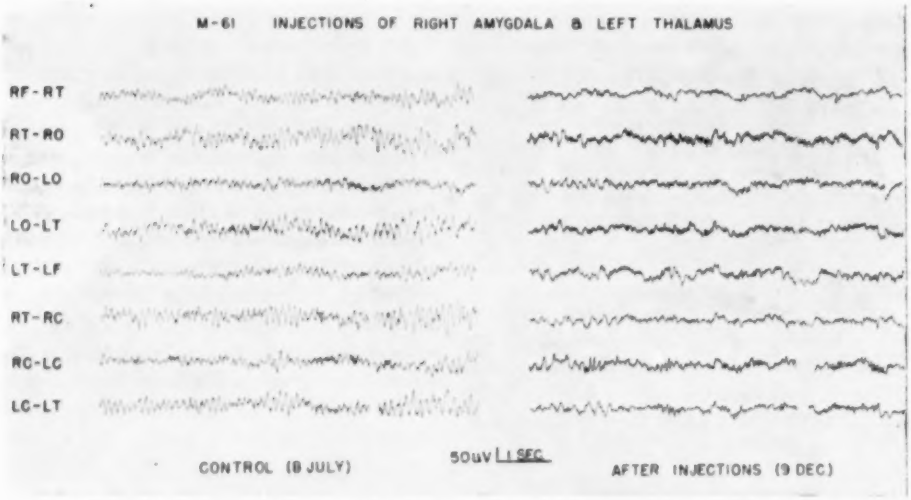

Fig. 3.—Electroencephalogram of Monkey M-61, showing at the left a sample of the control trace on July 8, demonstrating a dominant frequency in the alpha range. The animal then received an injection of alumina cream in the right amygdala (July 29) and the left thalamus (Oct. 28). The second trace (Dec. 9) at the right demonstrates the change in the dominant frequency to one in the beta range.

of the injection, although in one animal this became depressed after a few months. In one animal the dominant rhythm increased to the beta range.

Only two animals showed spontaneous electroencephalographic abnormalities; one (C-5) demonstrated six months following an injection in the right globus pallidus an asymmetry in the previously symmetrical bursts of bicentral sharp waves, those on the side of injection having a higher voltage. A second animal (C-12) demonstrated spontaneous bursts and runs of high-voltage sharp waves, reversing on the left central lead six months after injection of the left putamen and globus pallidus (Fig. 2).

In the one animal with a mesencephalic lesion, the preliminary beta activity and the biparietal spikes were depressed after the injection on the side of injection.

These electroencephalographic changes, in general, would fit into the current theses regarding the influence of the bulbar and thalamic reticular systems upon the spontaneous cortical activity. Figure 3 illustrates an example of this change in dominant frequency following injection.

3. Four animals developed an altered response to pentylenetetrazol activation. In two instances (M-62 and C-14) an increased nonfocal sensitivity promptly produced a generalized convulsion, six weeks and seven months after injections of the left amygdala and right globus pallidus and putamen, respectively. In a third animal (C-1) a similar, but less definite, alteration occurred six weeks after injection of the right mesencephalon and pons. In one Cebus monkey (C-2), six and one-half months after injection of the right thalamus, there was a definite increased sensitivity to the drug with the production of a generalized seizure, followed by postictal slowing in the right frontal, temporal, and central leads and then isolated spiking in the right central area.

4. None of the seven animals in which acute multiple subcortical recording experiments were performed demonstrated any clear abnormality in subcortical electrical activity.

Summary of Results of Subcortical Injection of Alumina Cream

Monkey	Site of Injection	Period of Observation	EEG Abnormality	Metrazol Activation	Route of Injection and Comment
M-61	Left thalamus Right amygdala	5 mo.	Beta activity; decreased biparietal bursts; transient right central spikes; depressed alpha	No change	Bilateral frontal trephines
M-62	Right thalamus Left amygdala	7 mo.	Beta activity	Slightly increased nonfocal sensitivity	Bilateral frontal trephines
C-1	Right substantia nigra & mesen. & pont. retic. subst.	12 mo.	Ipsilateral depression	Increased (?) sensitivity	Right frontal Turkel trephine; subcortical recording
C-2	Right thalamus (VA, VP, & VL)	14 mo.	Increased alpha & biparietal bursts on right	Increased sensitivity, focal (?)	Right frontal Turkel trephine; subcortical recording
C-3	Left amygdala-hippocampus	6 mo.	None	No change	Left frontal Turkel trephine
C-4	Right thalamus *	3 days			Right temporal Turkel trephine; died 3 days after injection
C-5	Right globus pallidus *	6½ mo.	Increased spikes, right central area	No change	Right temporal Turkel trephine
C-6	Rt. temp. cortex; base of putamen & nucleus basalis	14 mo.	None	No change	Right temporal Turkel trephine; subcortical recording
C-7	Left amygdala	5 wk.	None	No change	Left frontal Turkel trephine; died 5 wk. after injection
C-8	Left amygdala	6½ mo.	None	No change	Left frontal Turkel trephine; subcortical recording
C-9	Left amygdala	6½ mo.	None	No change	Left temporal Turkel trephine
C-10	Rt. globus pallidus & putamen	7¼ mo.	Transient right central spiking	No change	Right temporal Turkel trephine
C-11	Left putamen & amygdala	5 wk.	None	No change	Left frontal Turkel trephine subcortical recording
C-12	Left globus pallidus & putamen	6½ mo.	Increased frequency & left central spiking	No change	Left temporal Turkel trephine; subcortical recording
C-13	Hypothalamus *	5½ mo.	None	No change	Midline frontal Turkel trephine
C-14	Right globus pallidus & putamen	7¾ mo.	Transient right central spike; then R. depression	Increased nonfocal sensitivity	Right temporal Turkel trephine

* Histological confirmation not obtained.

The accompanying Table presents a summary of the results in chart form.

Comment

In 1931 Dusser de Barenne and Sager [1] aroused interest in subcortical stimulation when they described transient hyperesthesia, hyperalgesias, and probably painful paresthesias following intrathalamic injections of strychnine. Since then, various methods of excitation have been employed, with indifferent success. When Kopeloff and his associates discovered the potent epileptogenic effect of alumina placed on the motor cortex, several investigators seized upon the possibility of stimulating subcortical structures with this agent. Whittier et al.,[9] in 1949, noted the development of apparently painful paresthesias of the extremities three weeks after the injection of 0.05 cc. of alumina into the centromedian nucleus of the left thalamus of a macaque. The lesion was largely cystic, and the paresthesias were apparently relieved by bilateral postcentral cortical ablation. No electroencephalograms were made. The following year Kopeloff et al.[8] injected 0.1-0.2 cc. of an alumina preparation into the subcortical nuclei of 10 rhesus monkeys. Four animals developed seizures 1¼, 2, 7½, 11, and 12 months after injection into the medial thalamus bilaterally, the putamen bilaterally, the white matter adjacent to the cingulate sulcus on one side and the subcallosal fasciculus on the opposite side, and the subcallosal fasciculus unilaterally. The electroencephalographic pattern was said to be abnormal in nine of the animals, and the seizures produced tended to be bilateral. Several other injections of various subcortical groups failed to give rise to attacks.

In 1953 Gastaut et al.[6] produced seizures in a cat following the injection of 0.1 cc. of alumina cream (standard not given) in the lateral nucleus of the left amygdala. The attacks could be induced by pentylenetetrazol U. S. P. (Cardiazol) and controlled by Methylphenylethyl hydantoin (Mesantoin) and were accompanied by a 4-per-second sinusoidal rhythm, beginning in the left hemisphere. In a subsequent report [5] they claimed to have produced similar results in the "majority" of some 20 cats with injections of the amygdala-hippocampal complex. The seizures and electroencephalograms were similar to those induced by electrical stimulation of the same area and analogous to temporal lobe seizures in man. They did not indicate the length of the latent period before these seizures occurred.

The preparation which we employed in this study is known to have a latency of 6 to 12 weeks when placed in the motor cortex,[2] and it would seem reasonable to assume that a period of observation twice this long would be sufficient to develop some evidence of epileptogenic activity were this to occur. However, of the animals which Kopeloff et al. injected, two did not develop their attacks for some 11 or 12 months, which is longer than most of our animals were followed, although three were followed for even longer periods without seizures ensuing. Furthermore, the most definite electroencephalographic abnormality developed only four to five months after the injection, so that, while the average period of observation was only somewhat over seven months, we felt that this was sufficient. Although seizures are apparently readily produced by amygdala injection in cats, according to Gastaut et al.,[5] our results in the monkey were disappointing. In this series, seven animals had lesions involving the amygdaloid complex; none of these developed seizures.

Recently Kennard [7] has indicated that there may be an inherent epileptic susceptibility associated with certain electroencephalographic patterns. She has noted in monkeys a synchronous bilateral high-voltage discharge, occurring principally in the central and parietal areas, which has previously been referred to as bursts of biparietal sharp waves, and considered as normal. She believes that these bursts have epileptic potentialities. In analyzing our data in this study, we found that localized spiking in the central area occurred in five animals in

association with these biparietal bursts, a finding which may favor Kennard's hypothesis.

In conclusion, it must be stated that, in our hands, the use of alumina cream, in doses known to produce chronic cortical epilepsy, has consistently failed to produce subcortical seizures in monkeys. The reason for this failure in the light of the published data of others is not entirely clear. Possibly the observation period (seven-month average) was too short, but a technique which fails to produce results within that period is not a practically useful one. Perhaps a more concentrated preparation might be effective, since it is known that the convulsive threshold of the basal structures, as determined by other techniques, is much higher than that of the cortex.

Summary

A standardized preparation of alumina (aluminum oxide) cream was injected into various subcortical nuclei in 16 monkeys, in amounts known consistently to produce seizures when placed on the motor cortex.

The animals were observed and serial electroencephalograms recorded, employing pentylenetetrazol U. S. P. (Metrazol) activation over a period of from 5 weeks to 14 months (average 7 months).

There were no spontaneous seizures. Eight animals developed spontaneous electroencephalographic alterations, and four demonstrated some increased sensitivity to pentylenetetrazol-induced seizures.

On histological study the lesions were found to lie in most of the principal basal ganglia and thalamus.

The Johns Hopkins Hospital (Dr. Walker).

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Cerebral Blindness

An Analysis of Twelve Cases, with Especial Reference to the Electroencephalogram and Patterns of Recovery

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Cerebral blindness, often called "cortical" blindness, may be defined as bilateral absence of light perception (under the usual conditions of testing) caused by disease of the cerebral hemispheres. The lesions involve the retrogeniculate portions of the visual system on both sides, either the optic radiations or the calcarine cortex or both. For the purpose of this study, fulfillment of the following clinical criteria was required: 1. The patient was totally blind. 2. The eyes themselves (that is, media, retina, and optic nerve) were normal or showed only minor abnormality, incapable of causing blindness. 3. The pupillary light reactions were normal. 4. There was other evidence of bilateral cerebral disorder, either at the time the blindness developed or in the past. The limitations of these criteria will be discussed later.

This entity is well known, and many cases have been reported since the classical paper of Förster in 1890.[11] These reports have usually emphasized the pathology of this condition, and many concerned themselves with the denial of blindness (Anton's syndrome) that frequently occurs. Although denial of blindness was once believed to be a specific dysfunction relating to the visual system, Redlich and Dorsey[24] and, more recently, Weinstein and his associates[33,34] pointed out that it is merely one facet of the entire syndrome of denial of illness. The combination of disturbed consciousness and blindness may give rise to denial of blindness, no matter whether the visual loss is central or peripheral.

The usual cause of cerebral blindness is bilateral encephalomalacia in the calcarine cortex and subcortical white matter due to bilateral vascular occlusions, usually of the basilar and/or posterior cerebral arteries.[27] Sometimes one middle cerebral artery and the opposite posterior cerebral artery are occluded on different occasions. Brain injury is a relatively frequent cause of this uncommon condition.[26,29] Carbon monoxide poisoning has been present in some cases,[13,31] as has a rare cortical degeneration (Heidenhain's syndrome).[21] In one case an embolus lodged at the bifurcation of the basilar artery into the two posterior cerebral arteries.[15] Progressive subcortical encephalopathy (Schilder's disease) was responsible for a few cases, and there have been at least two cases of bilateral occipital lobe abscess.[14] Other causes include cerebral angiography[10]; neoplasms, regardless of location, causing increased intracranial pressure and presumed obstruction of the posterior cerebral arteries[9]; blood transfusion[25]; corticotropin[19]; ventriculography[25]; syphilis,[6] and meningococcal meningitis,[30] and as a transient phenomenon in electroshock therapy with the electrodes placed over the occiput.[28] In a few cases the cause was unknown.[5,37]

Although there is no typical syndrome, in most of the cases the onset was abrupt, with immediate blindness or severe visual defect leading shortly to blindness. The patient

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may deny that he is blind, but his observed behavior and responses to testing indicate that he has no vision. The eyes themselves and the pupillary light reactions are normal. There are other signs of bilateral cerebral disease, usually mental changes and hemimotor or hemisensory syndromes. The average case terminates in death in weeks or months, although some recoveries have been reported, predominantly in cases of traumatic lesions.

Although the relation of the EEG to vision is well known, and the brain wave patterns have been studied in blindness due to other causes, there is almost nothing in the literature concerning the relationship between cerebral blindness and the EEG. Subjects with congenital or acquired blindness due to disease of the eyes, optic nerves, or optic chiasm have normal EEG's (provided the brain is not also affected, although the alpha rhythm does not respond to opening and closing of the eyes. In homonymous hemianopsia there are often, but not always, alpha abnormalities referable to the hemisphere affected [4,16]).

Flickering light has been used to influence the brain waves in subjects with hemianopsia,[23,32,36] but differences between the responses of the two hemispheres, although suggestive, were not consistent. The problem requires more study.

The present study concerns the clinical aspects of 12 cases of cerebral blindness, with particular emphasis upon the EEG patterns in the acute phase, during recovery, and in response to intermittent photic stimulation. It was also possible to study certain associated phenomena, such as the behavior of optokinetic nystagmus and the sense of ocular position. The problem of visual agnosia was considered in relationship to blindness, and the differentiation of cortical and hysterical blindness is briefly discussed. The relationship between the actual loss of tissue in the geniculocalcarine system and the loss of function which occurs is not a simple one, and the resulting physiological implications are considered.

Material and Methods

The subjects were 12 patients with cerebral blindness. They fulfilled all of the criteria listed in the introduction. The probable causes were as follows:

1. Bilateral cerebral infarctions due to arterial insufficiency (Cases 5, 7, 8, 9, 10)
2. Cerebral venous occlusion (Case 2)
3. Progressive subcortical encephalopathy (Case 6)
4. Hodgkin's disease (Case 12)
5. Carbon monoxide poisoning (Case 3)
6. Trauma (Case 4)
7. Intracranial hemorrhage with hypertension and nephritis (Case 1)
8. Recent arterial occlusion on one side and old trauma to the opposite occipital lobe (Case 11)

All the patients had EEG's. In most cases the effect of eye opening and closing and responses to a steady light were recorded. In six cases it was possible to study the responses to rhythmic photic stimulation, using a stroboscope at 12 in. (30 cm.) from the eyes. Both the Buffington* and the Grass† photic stimulator were used in these patients. Stimulation was given at frequencies of 1-21 flashes per second, and in some cases it was possible to observe the effect of varying the position of the light in the visual field. "Response" to flickering light was defined as the presence of a well-defined sinusoidal rhythm in the EEG at the same frequency as the stimulus (or at an exact harmonic or subharmonic frequency), synchronous with it, and appearing and disappearing when the stimulus light is turned on and off. Responses from the frontal areas (rare in this series) were looked upon with suspicion as probable artifacts and therefore not considered. Naked-eye analysis only was used, and it is not known what electronic methods of analysis might have shown under the same circumstances.

Seven patients died. Of the five that survived, none remained blind, and it was possible to make serial studies of the returning vision, the EEG, and the responses to flickering light. Optokinetic nystagmus and the sense of ocular position were also noted. In three cases the postmortem findings were available for study, and will be referred to briefly.

Results

Clinical Features.—Total blindness usually came on suddenly (Cases 1, 2, 3, 4, 5, 7, 9, 10, and 11). In one case (Case 9) there

* Buffington Electronics, Inc., Cleveland.

† Grass Instrument Co., Model PS-1, Quincy, Mass.

had been temporary episodes of blindness prior to the final, permanent attack. Violence accounted for the sudden onset in two cases—the one instance of trauma (Case 4) and of illuminating gas poisoning (Case 3). In one (Case 12), a patient with a long illness, the blindness was discovered by examination before there was any visual complaint. In only two cases was there a history of gradual, progressive blindness (Cases 6 and 8). It was presumed in five cases that a homonymous hemianopsia had been present for some time before the final onset of blindness, and that the total loss of vision was the result of recent homonymous hemianopsia on the opposite side.

In the five cases that recovered the patterns of return of vision were variable. In one (Case 1) it came back so rapidly that only limited observations could be made; the transition from total blindness to good, useful vision occurred within 48 hours. In the remaining cases there was a fairly typical pattern. Vision returned very slowly, and the mental state or the presence of aphasia often made the actual course difficult to assess. None of these four patients has yet made a complete recovery of vision. Details of the visual studies are given in a subsequent section.

Associated Findings.—Every patient had definite neurologic signs outside the visual sphere. These included mental changes and motor and sensory defects, depending on the location and extent of the major pathologic changes. The mental symptoms consisted of frank psychotic behavior, defects in communication, disorientation, confusion, memory deficits, and abnormal states of consciousness from lethargy to stupor.

Denial of blindness was common. Seven of the twelve patients showed explicit or implicit ‡ denial at some time during their illness. Only two patients consistently admitted they could not see, and neither one could be observed carefully enough (one died shortly following admission, and it was impossible to communicate satisfactorily with the other over a long enough period of time). In two patients it was impossible to determine (one was a child, and the other was psychotic during the period of blindness). The incidence of denial in this series is very high (58%). In hemiplegia, Nathanson, Bergman, and Gordon[22] found that 25% of the patients denied their paralysis. However, implicit denial was not included in that study, and there was a high proportion of patients with aphasia too severe to permit testing of "explicit" denial.

The course of this symptom was studied in detail in one patient (Case 10), as it fluctuated considerably. It was observed that his disorientation and denial of blindness came and went together. When he was most confused, the blindness was denied and he confabulated during visual testing. At other times he was quiet and fairly well oriented, admitting his blindness and accepting it as his chief reason for coming to the hospital. The relationship between denial of illness and orientation was commented on by Redlich and Dorsey[24] and repeatedly emphasized by Weinstein and his associates.[33,34]

EEG Findings.—Electroencephalographic studies were performed during the period of blindness in every case, and the findings are summarized in the accompanying Table. When the patient was blind, there was no occipital alpha activity in any case, and only two cases had any alpha waves at all. In one of these (Case 4; Fig. 1) the basic rhythm was present in both frontal and motor electrodes and in the left parietal electrode, but not in the right parietal or in either occipital electrode. In the second case (Case 9) there was some alpha activity in the right motor-parietal area, but nowhere else. Alpha activity was absent in the other

‡ These terms, taken from the studies of Weinstein and Kahn,[35] are defined approximately as follows: "Explicit" denial is the actual denial of blindness in so many words, in conjunction with other behavior (confabulations of things seen, for example), suggesting denial. In "implicit" denial, although the patients admitted blindness when asked specifically whether they could see, their spontaneous speech and actions indicated that they denied or minimized the defect.

Case No.	Alpha Activity	Slow Waves	Other Abnormal Activity	Response to Steady Light or Eye Opening	Response to Flickering Light
1	Absent	Diffuse with bursts, more on right	Spikes, right paneto-occip.	None	None
2	Absent	Diffuse, left more than right	Low voltage on left	None	--
3	Absent	Diffuse & symmetrical	None	None	None
4	Present in frontal & motor electrodes; absent posteriorly	Diffuse	None	None	--
5	Absent	Focal (right side)	None	None	--
6	Absent	Diffuse & symmetrical	None	None	--
7	Absent	Diffuse; symmetrical posteriorly, more on left anteriorly	None	--	--
8	Absent	Diffuse, accentuated in right temporal	None	None	None
9	Only in right motor-parietal area; absent elsewhere	Diffuse & symmetrical	None	--	--
10	Absent	Diffuse & symmetrical	None	None	--
11	Absent	Diffuse, accentuated in right temporal-occip.	None	None	--
12	Absent	Diffuse, more on right side	None	None	--

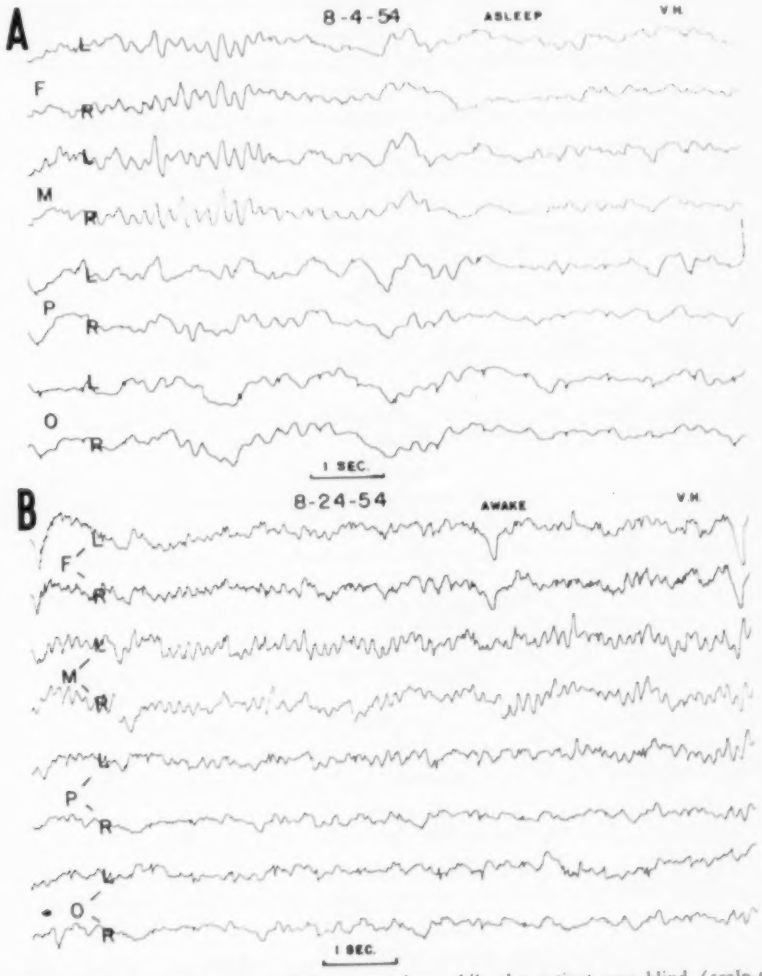

Fig. 1 (Case 4).—Electroencephalograms taken while the patient was blind (scalp-to-ear combinations).

(*A*) Asleep. The record is unremarkable for a child of this age.

(*B*) Awake. An alpha rhythm at 8 cps appears in the frontal, motor, and right parietal areas but is absent posteriorly.

10 cases. In four of the five patients who recovered alpha returned, so that (at least in these cases) its absence was not simply a normal variant. Unfortunately, only one (Case 8) of the four patients who became blind under observation (Cases 1, 6, 8, and 12) had EEG's taken prior to the onset of blindness. In this patient (Fig. 2) some alpha activity was present before complete blindness resulted, and this disappeared simultaneously with loss of vision. Aside from the behavior of the alpha waves, there was nothing to distinguish these records from those of other patients with severe cerebral disease. There was slowing in every case, and frequently marked differences in voltage between the two sides, but the findings were consistent with the location and severity of the clinical abnormalities. When the patient was blind, neither

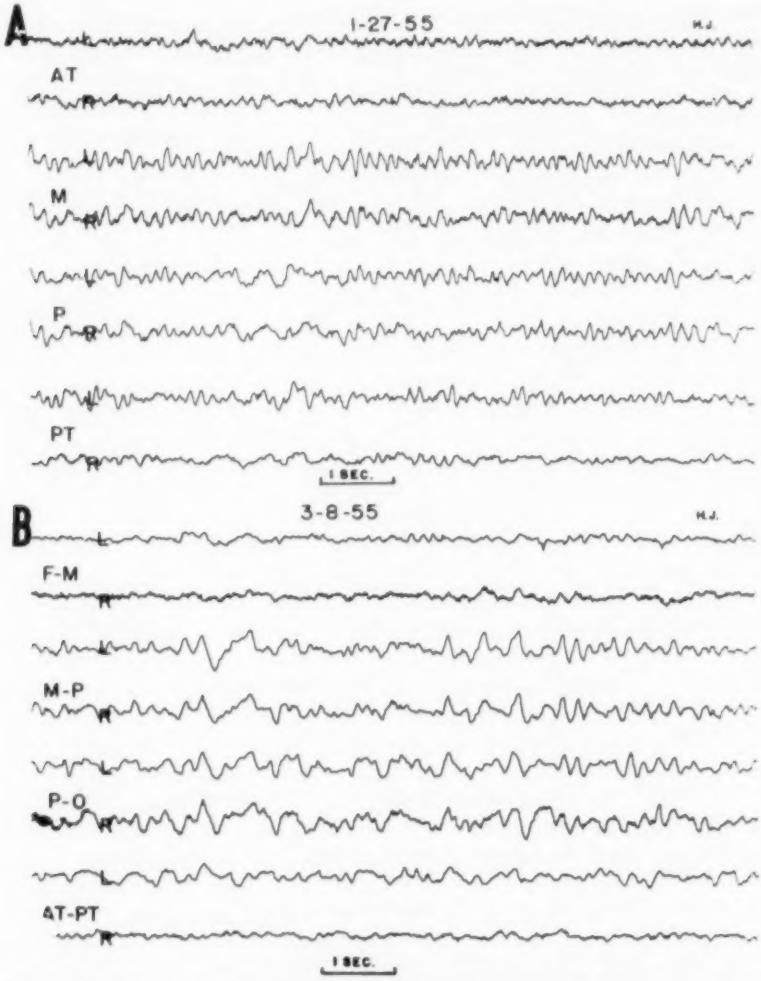

Fig. 2 (Case 8).—(*A*) Scalp-to-ear combinations. The patient still has some vision at this time. Alpha activity at 8 cps is generally present, although it is not seen at the right posterior temporal and (not shown) occipital electrodes.

(*B*) Scalp-to-scalp combinations. The patient is blind at this time. No alpha activity appears, and there is more slowing.

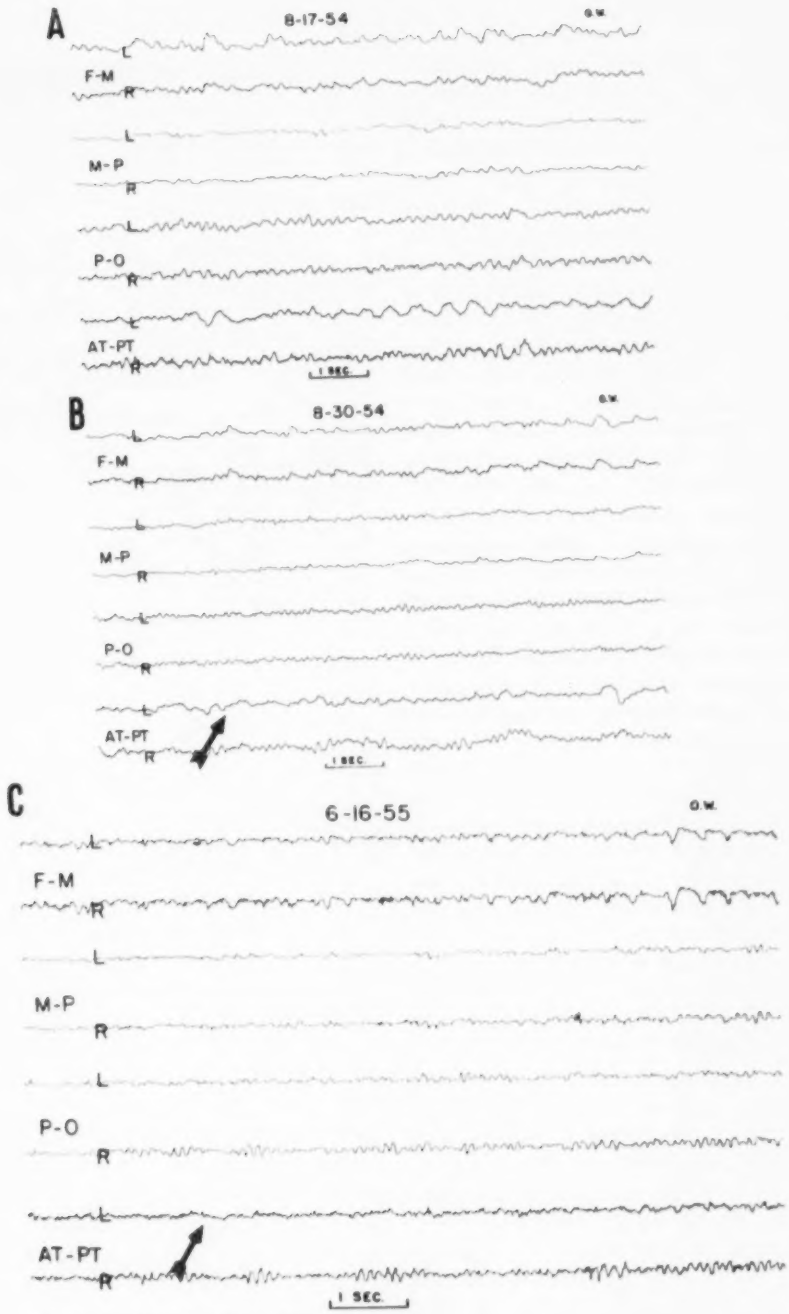

Fig. 3 (Case 2).—Scalp-to-scalp combinations.

(*A*) Just before the return of vision. There is no alpha activity, although there are a few waves in the alpha range in the right temporal area, with focal slow waves in the left temporal region.

(*B*) Some vision is present. Alpha activity has returned, but there is focal slowing and absence of alpha rhythm in the left temporal area (arrow).

(*C*) Ten months after the return of vision. The only abnormality is focal absence of alpha activity in the left temporal region (arrow).

opening or closing the eyes nor continuous or intermittent light stimulation affected the EEG. Of the patients that recovered, all responded to eye opening or steady light by blocking of the alpha rhythm, a normal response. Only two out of the four recovered patients showed any response to flickering light. Those that responded (Cases 1 and 3) were examples of diffuse cerebral disease, probably toxic-metabolic in nature. The other two (Cases 2 and 5) were examples of cerebral vascular disease with focal neurologic findings. (Patients with hemianopic field defects generally respond to flickering light bilaterally, and not all normal subjects do so.)

The pattern of the EEG during recovery consisted of a return of alpha activity with the return of vision (vision was present before alpha activity had reappeared in all four cases), and it ultimately assumed normal frequency and distribution. In one of the four cases (Case 2; Fig. 3) it remained absent from the left posterior temporal-occipital area long after vision was present (though defective) in both half-fields. In this case the side in which alpha activity remained absent (left) corresponded to the clinical neurologic picture (aphasia and predominant defects in the right homonymous field). Over the course of time, the slow activity decreased in amount and increased in frequency. One patient's record became completely normal (Case 1); the other four records were still abnormal 7 to 12 months after the onset of blindness.

The consistency of the EEG findings suggested a comparison with other conditions affecting the geniculocalcarine system, and with cerebral lesions not associated with visual field defects. The findings are illustrated in the graph (Fig. 4). In cases of hemianopsia, alpha activity was absent in 10%, focally absent in 70%, and present bilaterally in 20%. With diffuse or focal lesions not involving the visual system, the alpha activity was usually normal (90%). Thus, the patterns of alpha activity are strikingly different in the various groups.

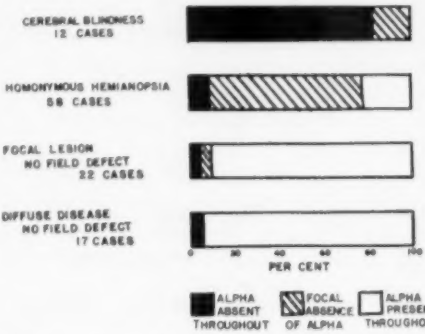

Fig. 4.—Types of alpha abnormality in various conditions affecting the brain. In cerebral blindness there was complete or focal absence of alpha activity in every case, usually the former. In homonymous hemianopsia alpha activity was absent in a small number of cases; in most of the others it was absent focally. In 20% of cases it was essentially normal (that is, approximately equal bilaterally). In lesions without field defects alpha activity was either bilaterally present or, less commonly, completely absent. (Alpha rhythm may be absent, of course, in normal subjects.)

Although a relationship between alpha rhythm and disease of the geniculocalcarine system is obvious, the 20% of cases of hemianopsia in which alpha activity is unaffected have to be explained. Whether the explanation is anatomical (location of the lesion) or lies in some other factor cannot be determined from the facts at hand. This problem is discussed later.

Postmortem Observations.—Autopsy was performed in three of the seven patients that died. All showed almost identical findings in the occipital lobes, similar to those of Case 8 (Fig. 5). There was virtually complete destruction of the calcarine cortex on both sides. The subcortical white matter was relatively unaffected, although there were scattered areas of encephalomalacia elsewhere in the brain. In all of these cases the cause was arterial occlusion due to arteriosclerosis. The posterior cerebral arteries were involved in every case; in one it appeared that the original lesion was in the basilar artery, with the posterior cerebral distribution secondarily affected. In general, these lesions resemble those reported in the literature in cases of cerebral

Fig. 5 (Case 8).—Both calcarine cortices are destroyed, although the poles are preserved. In addition, there are large softenings in the right temporo-occipital cortex and smaller cavities in both putamens. (There were also scattered softenings in the pons.) The underlying pathologic process was an almost complete occlusion of the upper end of the basilar artery by arteriosclerotic deposits.

blindness. (Incidentally, very few postmortem studies are available in the literature.)

Patterns of Recovery of Vision.—The earliest sign of recovery was appreciation of light in the central field of vision. By the time the patients could be adequately tested, there was usually an island of central vision, in which acuity was fairly good; optokinetic nystagmus could be elicited (at least in one direction), and colors could be identified in a good light. (However, if the illumination was reduced, color perception could be abolished.) The preserved central field of vision was usually unequal in the two homonymous half-fields. One patient could identify objects by name in the central visual field before it was certain that she could tell accurately whether a light was on or off, and before accurate color recognition was present. (In Wechsler's case,[31] color vision returned before the appreciation of form. This could have been an agnosic disturbance.) At least in this case, this suggests that the essential defect is in visual perception at a "low" level, rather than severe visual agnosia. Bramwell[3] made a similar observation.

When more peripheral vision returned, one homonymous half-field or quadrant was usually "better" than the other, although not always in the same respect. For example, in one patient (Case 2) motion was perceived poorly and objects could not be localized accurately in one homonymous half-field, whereas color recognition was good. In the other homonymous field, color recognition was grossly defective and there was extinction of stimuli when presented simultaneously with objects on the opposite side.

In one case (Case 1) recovery of vision occurred so rapidly that adequate serial studies could not be done. It was observed, however, that the perception of colors was the last function to return, although no fields could be plotted by means of color. Even when testing with colors showed no defect, he persistently reported the walls of his room as "gray," when they were a light grayish-green. A week later he was consistently correct.

All of the patients tested showed varying degrees of inability to perceive the position of their eyes and had difficulty with gaze movements on command. Although aphasia may interfere with the evaluation of this phenomenon, it could be clearly shown when there was no right-left confusion, and the patient could follow commands involving other parts of the body. In one patient this defect disappeared when the vision returned to normal, remained unchanged in those who failed to regain any vision, and improved, though not completely, in patients who remained with some visual defect. This finding emphasizes the dominant role of vision in ocular position sense and is consistent with related observations in this field.

Optokinetic nystagmus could not be elicited in any blind patient. With recovery, optokinetic nystagmus was variable, but usually it could be demonstrated when the stripes were coming from the direction of the intact field and was absent when they were coming from the defective field. The difference between optokinetic nystagmus in the two directions is not simply a perceptual defect, since it occurs in frontal lobe lesions and is absent in lesions affecting the optic tract. The opticomotor system must also be damaged to produce this defect.

Responses to Rhythmic Light Stimuli.—Two patients (Cases 1 and 3) were studied while completely blind; these, and two additional patients (Cases 2 and 5), were examined repeatedly during the course of recovery. EEG responses to flickering light were absent during blindness and returned when some vision was regained. Both gave responses only with their eyes open and in this respect behaved like our normal subjects. Although some normal persons give responses in the EEG with their eyes closed, there is an EEG response in almost every subject when he has his eyes open and fixates the light. If the subject's gaze deviates only a few degrees from direct fixation, the responses cease. It is not surprising, then, that two patients gave no response, even though some vision had returned, since they could not fixate the light adequately. (This may be comparable to what occurs in optokinetic nystagmus. Since fixation of some sort is required for optokinetic nystagmus, it can be abolished voluntarily by relaxing the muscles of accommodation, but usually can be elicited in subjects who are not deliberately attending to all details of the stimulus, such as uncooperative humans and monkeys. In our patients, optokinetic nystagmus had returned in some instances where flicker responses did not occur, but not the reverse.)

Report of Cases

Case 1.—*Clinical Summary.*—The illness in this 44-year-old man was characterized by fluctuating blindness with retention of pupillary reactions, varying degrees of stupor, hemiparesis, and grand mal seizures. There was gradual recovery to complete normality. The cause was not determined, but there were hypertension, uremia, leukocytosis, and blood in the urine.

EEG Observations.—While the patient was blind there was no alpha activity, and the record showed diffuse slow waves, including paroxysmal forms, more prominent on the right. There were sporadic spikes in the right parietal-occipital area. There was no response to steady or flickering light or to opening and closing of the eyes. With recovery, sparse, then abundant, alpha waves appeared at 9 cps. Bursts persisted, again more prominent on the right. There was a response to steady light and to flickering light in a normal pattern.

Case 2.—*Clinical Summary.*—This 31-year-old woman developed convulsions, with stupor and coma, accompanied by bloody cerebrospinal fluid, during the last trimester of her fifth pregnancy. She became completely blind, but the pupils reacted normally to light and the optic fundi were normal. A carotid angiogram did not reveal the cause of the intracranial bleeding.

The patient's condition suddenly improved about three months after admission, and it was possible to perform visual field examinations, using hand motion. At this time she showed a left homonymous hemianopsia with preservation of central vision. She was frankly aphasic but cooperated in examinations. The remainder of the neurologic examination was essentially normal. Ten months after onset (seven months after the return of vision) an examination showed the following: Her vision was poor, so that she could not go out in the street alone; but it was difficult to test because she was also aphasic. On gross field testing, there was a persistent mislocalization of objects in the left homonymous field, and she perceived motion less well in these fields. However, in the right homonymous field there was defective color perception, and she persistently extinguished objects in her right field when presented simultaneously with objects on the left. Optokinetic nystagmus was present from left to right, but not from right to left. She could not look in any direction on command, and did not know accurately the position of her eyes (both these observations could have been incorrect, owing to the patient's aphasia).

The latest observations, made one year after onset, showed that her vision was somewhat better, and finger counting was improved in both eyes. In the right homonymous field, objects seemed to be farther away, and she localized them poorly. Color perception was worse on the right. On the left side there was extinction of double simultaneous stimuli, and perception of movement was worse on the left side.

EEG Observations.—When she was blind, there was no alpha activity, and the record consisted of slow waves, slower on the left, with a general reduction of voltage throughout the left side (Fig. 3*A*). Two weeks later some vision had returned and alpha activity at 9-11 cps began to appear, although it could never be seen in the left posterior temporal area (Fig. 3*B*). As time went on, alpha activity became more prominent; the slow waves were reduced in prevalence and were not so slow. However, 12 months after onset, alpha activity remained absent in the left posterior temporal area (Fig. 3*C*), and there was no response to flickering light, although alpha blocking occurred normally in response to a steady light or to eye opening.

CASE 3.—*Clinical Summary.*—This 19-year-old woman attempted to commit suicide with illuminating gas. When she was able to be tested, she was found to be blind, with preserved pupillary reactions and normal fundi. She had weakness and contractures of all four extremities.

There was no unequivocal evidence of visual perception until five months after the start of the illness. A month later there was light perception in both eyes. On the left vision was detectable only in the temporal crescent; in the right eye some central vision was present, and she seemed to be able to perceive motion there. Optokinetic nystagmus was absent. The pupillary reactions and fundi were normal. Six months after onset she recognized color. She had difficulty in appreciating the position of her eyes. Eight months after onset she could count fingers in the central field at 1 to 2 ft. (30 to 60 cm.). There was movement perception in the periphery. It was reported that red and yellow were recognized correctly, but she made mistakes in recognition of blue and green. Nine months after onset, she apparently had some vision in the left half of the visual field, and some indefinite localization in the right field. She was very labile emotionally. At times she said that she could not see anything. She recognized many objects, but occasionally failed to recognize anything for a period of time. Pupillary reactions were normal. She did not know the position of her eyes in space. She had a right-left confusion, but, in addition, there was defective perception of her eye position. Eleven months after onset her vision improved. She recognized people instantly, but detail vision was very poor, and she still confabulated many details. She still had a markedly defective right-left orientation, and this made it difficult to test ocular position sense. There were still defects for form, motion, and color, more marked on the left than on the right; but she often made mistakes on the right as well. The visual field appeared to be limited to a small central field, but it was impossible to determine the exact limits of the visual fields. She got most color responses correct in the central field, but she made mistakes on light colors, particularly yellow and green, and on some of the dark colors, particularly red.

EEG Observations.—During the period of complete blindness, the EEG was a low-voltage, characterless record, with sparse activity of any kind and no alpha waves. Alpha waves appeared almost simultaneously with the return of vision. Diffuse slow waves were present. There was no response to flickering light even after alpha activity had become normal in respect to distribution and in response to steady light and eye opening.

CASE 4.—*Clinical Summary.*—This patient, 15 months of age, was admitted to Bellevue Hospital because of a severe head injury on the day of admission. On admission, he was conscious but drowsy. There was a palpable depressed fracture in the right parieto-occipital area. The eyes were deviated to the right and downward. The pupils reacted to light, but the patient was apparently completely blind. X-rays of the skull confirmed the impression of a compound depressed fracture of both occipital bones and the right parietal bone. A lumbar puncture showed grossly bloody fluid under a pressure of 300 mm. An operation was performed a week later because of the patient's failure to improve, and it was found that both occipital lobes were severely lacerated, the right more than the left. Vision did not return until one month after the injury, but six months later vision was normal insofar as it was possible to test it.

EEG Observations.—During the period of blindness (Fig. 1*B*) there was 8-per-second activity in both frontal and motor areas and in the left parietal area. None of this activity appeared in the right parietal area or in either occipital or temporal area. There were diffuse slow waves at 2-5 cps, slower on the right than on the left. A steady light in the eyes did not affect the record. The effect of opening and closing the eyes could not be studied accurately. A sleep record was essentially normal except for decreased amplitude posteriorly on the right side (Fig. 1*A*).

CASE 5.—*Clinical Summary.*—This 45-year-old man was admitted because of sudden blindness four hours previously. A year ago he had had acute hemiplegia with a hemisensory defect. This cleared after an undetermined period of time, and he was apparently well until four hours prior to the present admission, when there was a sudden onset of blindness. The blindness was variably denied and admitted by the patient. He was known to have had hypertension for many years.

On admission, he was disoriented and somewhat agitated. Neurologically, there was no light perception, but the pupils were equal and reacted

normally to light. The optic fundi were normal. The left corneal reflex was absent, and he had a spastic left hemiparesis and hemisensory defect.

A month later he had regained some vision, so that it could be tested adequately. At this time the central visual field was the only field preserved, with fairly good acuity in it (about 20/80). Optokinetic nystagmus was present to the right and absent to the left. Following movements were normal to the left but saccadic to the right.

Six months after onset vision was limited to a small central tube in each eye, with no striking differences between the right and left halves of the fields of vision. Color perception was poor bilaterally but did not seem to involve any special colors. In a good light, color identification was perfect, but under slightly reduced illumination color identification was absent. Central vision was fairly good to gross testing. There was optokinetic nystagmus to the right, but not to the left. Following movements to the left were smoothly performed, but to the right they were performed in a jerky manner. Macular vision was not completely preserved; at a distance of about 15 ft. there was evidence of involvement of the central field, in that when looking at a face he saw only one ear, the one on the right side of his field of vision. There was still a left hemiplegia, and the other neurologic signs remained the same. Using the HRR pseudoisochromatic plates,§ the patient identified no colors consistently except bright red, and occasionally bright green, and did not recognize the shape of colored objects. There was no pattern as to the distribution of the objects that he did see.

EEG Observations.—When the patient was blind, alpha waves were absent, and slow waves appeared throughout the right hemisphere. Alpha activity had not returned with the recovery of vision, but five months later alpha, at 8-9 cps, was well organized and slow activity, although less, was present in the same distribution. Flickering light did not affect the record, although eye opening induced alpha-wave blocking.

Case 6.—*Clinical Summary.*—This boy of 10 years was admitted because of defective vision, unsteady gait, and mental changes, of seven months' duration.

On admission, his speech was mostly gibberish. He was deaf and completely blind. The pupils were normal in size and reacted normally to light. There was a bilateral Babinski sign. A pneumoencephalogram showed essentially normal findings. Shortly before his death, 8 months after admission and 15 months after the onset of the illness, the eyes moved constantly up and down in a coarse rhythm. No lateral gaze could be elicited by rotating the head. Tonic neck reflexes were present, so that rotation of the head to the left produced flexion of the right leg and arm. Rotation to the right, however, produced no response. Somewhat later he had convulsive seizures and died.

EEG Observations.—During complete blindness the waking record showed no alpha activity and eye opening had no effect. The sleep record was unremarkable for the patient's age.

Case 7.—*Clinical Summary.*—This patient, aged 49, was admitted to the hospital because of onset of sudden blindness three weeks prior to admission. Six months before she had sustained acute right-sided paralysis with difficulty in speech. This cleared over the course of the next two months. She was apparently normal until three weeks prior to admission, when she suddenly complained that she could not see at all.

On examination, the patient was found to be totally blind. However, the optic fundi were normal, and the pupils were equal and reacted well to light. There were some defects in language function and right hemiparesis with increased reflexes on the right side. The eyes showed no abnormal movements. The remainder of the examination was essentially normal.

There was no significant change in her condition until two weeks after admission, when cyanosis suddenly developed in the left lower extremity, and within two days she was dead, apparently of a pulmonary embolus secondary to femoral thrombophlebitis.

EEG Observations.—The only record was taken while the patient was blind. It showed no alpha waves, but was dominated by slow activity, accentuated on the left anteriorly.

Postmortem Examination.—The ventricles were slightly enlarged. There was softening of the gray matter and the underlying white matter on the medial aspects of both occipital lobes, with a smaller separate infarct in the left angular gyrus.

Case 8.—*Clinical Summary.*—This patient, aged 52, was admitted to the hospital because of progressively failing vision and frontal headaches of two months' duration.

On admission, there was a marked organic mental syndrome. Visual testing revealed light perception only in the right homonymous fields. The left half-fields were blind. The pupils reacted normally to light, and the fundi were not remarkable. The gait was slow and unsteady, but there were no other frank abnormalities in the neurologic examination.

§ The HRR plates (American Optical Company) are similar to the familiar pseudoisochromatic tests originated by Ishihara, that is, patterns differentiated from a background only by color, with brightness and other cues eliminated.

Shortly after admission, he was seen to have myoclonic twitchings of the left upper extremity. The eyes were held mostly toward the right and did not move to the left even on passive turning of the head. Dissociation of eye movements was induced by cold caloric stimulation of the ears. The patient became progressively more deteriorated, and all verbal contact was lost. He became totally blind, but the pupils reacted well to light. He continued to hold his eyes mostly to the right side. Eventually he became comatose and died.

EEG Observations.—The initial records were taken while the patient still had some vision (Fig. 2*A*). There was alpha activity, at 8 cps, with slow waves, lower and slower in the right temporal area. The alpha activity diminished in prevalence and disappeared at about the same time that the patient became blind (Fig. 2*B*). Slow waves became more prominent, still with the same focal accentuation.

Postmortem Examination (Fig. 5).—The essential findings were (1) almost complete occlusion of the upper portion of the basilar artery by arteriosclerotic deposits; (2) complete destruction of the calcarine cortex bilaterally; (3) encephalomalacia in two large areas of the right temporo-occipital cortex of the convexity; (4) scattered small anemic infarcts throughout the subcortical white matter and in the tegmentum and basis pontis.

CASE 9.—*Clinical Summary.*—This patient, aged 49, was admitted because of onset of sudden blindness six months previously. There was a history of hypertension for the past 13 years. He had had a "stroke" three years before, characterized by a defect in sensation and some defective vision on the left side; another "stroke" occurred six months prior to admission, with weakness of the right side of the body and difficulty with speech. At this time he became totally blind. He usually admitted that he was blind, but on a few occasions he said, "I thought I just saw mother; Where did she go now?" However, when asked immediately after this, "Can you see?" he answered, "No."

There was no change in the patient's condition during his hospital stay, and he was transferred to a state hospital two months after admission.

EEG Observations.—The only record was taken with the patient blind. Although there was some 10-11 cps activity, it appeared only in the right motor and parietal areas. None was seen in the occipital region, and none on the left side at all.

CASE 10.—*Clinical Summary.*—This patient, aged 72, was admitted to Bellevue Hospital because of two days of shortness of breath, coughing, and expectoration of blood-stained sputum. There was a past history of hypertension, and his wife stated that 18 months ago he had had a "stroke" and was blind "in the right eye" for one week. Seven days after admission the patient suddenly became blind and developed mental confusion.

Examination showed a mild organic mental syndrome, complete blindness without any ability to differentiate light and dark, and no reaction to threatening gestures. The pupils were equal and reacted to light. The fundi were normal. There were no motor or sensory findings, and he did not deny blindness.

A month after admission the patient stated that his vision was "just about normal". At this time he was completely disoriented for places and dates. He did not know where he was and denied being sick at all. He was able to point to parts of the body correctly, but he was unable to follow complicated commands. It was noted later that he denied blindness when he was most disoriented and complained of being blind when he was oriented, or approximately so. He stated that his vision had been "fine for the past few days." In the remainder of his stay, the patient became progressively more agitated. He remained disoriented and persistently denied blindness. There was defective awareness of the position of his eyes, and he made errors in right-left orientation. He became progressively more dyspneic; the heart failure increased, and he finally died, two months after admission.

EEG Observations.—The only record was taken with the patient blind. No alpha activity appeared, only diffuse slow waves. Opening the eyes had no effect.

Postmortem Examination.—The vessels at the base showed marked atherosclerosis, with only one well-developed vertebral artery. There was some cortical atrophy in the frontal and upper parietal region. There was bilateral softening of the medial and undersurface of the frontal lobes and of the calcarine cortex on both sides.

CASE 11.—*Clinical Summary.*—This 60-year-old woman was admitted because of sudden blindness. The only other reliable point in the history was a head injury approximately two years ago, for which she was not hospitalized and about which no other details were known.

On neurological examination, the patient was found to be totally blind, but she always insisted that she could see and confabulated about objects held in front of her. She was disoriented and had hallucinations and delusions throughout her hospital stay. The optic fundi were normal, and the pupils reacted normally to light. The ocular movements were normal. There was frequent blinking. There was no reaction to stimulation with the opticomotor drum.

A pneumoencephalogram showed diffuse dilation of the ventricular system with a large, air-filled cavity in the right occipital lobe.

Many of her spontaneous statements contained the words "see," "watch," and "look." Her status was unchanged throughout her hospital stay, and she had to be transferred to a state hospital.

EEG Observations.—The only EEG was taken with the patient totally blind. Alpha waves were absent. Slow waves appeared throughout, accentuated in the right temporo-occipital area. Opening and closing the eyes had no effect upon the record.

Case 12.—*Clinical Summary.*—This patient, aged 43, was admitted because of difficulty in walking of one week's duration. Seven years prior to admission a tumor in the chest was discovered, presumed to be Hodgkin's disease, and treated with radiotherapy. Four months previously she was admitted to the hospital and a positive diagnosis of Hodgkin's disease made on the basis of biopsy of a lymph node in the neck. Failing vision was first noted about this time, although no details were given. The vision became steadily worse, and two months prior to admission a pneumoencephalogram was taken, but was reported to be negative. In the three weeks prior to admission the patient became almost totally blind. One week prior to admission she was found to be almost unable to stand up and, when supported, had a tendency to fall in various directions.

On examination she was apparently totally blind. The pupils reacted normally to light, and the optic fundi showed no abnormality. She could look to the right, to the left and down, but not up. There was some nystagmus on lateral gaze in both directions, but it was not sustained. Later, she began to have gross swinging eye movements from the right to the left, and these became much more prominent as time went by. Her condition became progressively worse, and she died. Permission for postmortem examination was refused.

EEG Observations.—The only record was taken when the patient was blind. No alpha activity appeared. There was diffuse slow activity, more prominent on the right side. Opening the eyes had no effect upon the record.

Comment

Cerebral blindness is a rare condition, but probably not so rare as the few published case reports imply. Like denial of illness and many other disorders of perception, it has to be looked for specifically, as blindness is often denied and the vision of infants is notably difficult to assess, particularly if there are other manifestations of cerebral disease. A patient lying immobile in bed in a psychiatric hospital may be blind without even the physician's being aware of it.

Although the relation between vision and the EEG was noted by the discoverers of brain waves, cerebral blindness has not been studied by this means. One relevant case report is that of Cohn.[5] His patient, who eventually recovered, had EEG's while he was blind (this lasted only 24 hours) and periodically over the next 10 months. The patient, a man of 42, had a sudden onset of vertigo, tinnitus, blindness, and aphasia. This improved considerably in the next few days, but a year later there were still language defects. Recovery of vision occurred in the form of a central "hole" with eventual return of vision to normal. The EEG while he was blind showed bilateral slow waves, mostly posteriorly, and absence of alpha activity. Within a day (vision consisted of a central "hole" of light perception) there were sparse alpha waves, but they were central, not occipital, in location. The alpha activity increased, and the slow activity decreased progressively, until the records 10 months after onset showed alpha activity of normal distribution and no abnormal waves.

The sequence of events in this case was almost the same as in those of our patients who could be studied serially. Alpha activity was absent in every case when the patient was blind. Although this finding was consistent, the number of patients reported is small, and cerebral blindness is only one of many conditions that cause abolition of alpha activity. Absence of the normal basic rhythm is usually associated with severe damage to the brain, and is not necessarily related to defective vision. However, we often do not know whether vision is present in patients whose brains are severely damaged and who are in deep stupor or coma. Anoxia, edema, and other factors contribute to cerebral dysfunction in these conditions, and it is unlikely that the visual system escapes their effects. As pointed out above, there is certainly some relation between vision and the brain waves, especially the

alpha rhythm. All the cases of blindness and half the cases of hemianopsia showed bilateral or unilateral abolition of alpha activity, and (where it was possible to examine the relationship) the alpha activity reappeared with the return of vision or was abolished by the progress of the condition producing blindness. (An exception was reported by Williams and Reynell,[35] whose case showed normal alpha activity associated with complete cerebral blindness.) The importance of visual attention in responses to flickering light and in influencing the alpha rhythm suggests that these functions are related, although the nature of such a relationship is still in the descriptive stage.

The nature of the alpha rhythm is, of course, still a problem, but some relationship to the visual system certainly exists. In these cases, as well as in those with homonymous hemianopsia, disturbances of the alpha pattern occur which are not usually present in focal or diffuse cerebral lesions without field defects.[4,34] Jaffe and Bergman[16] studied cases of lesions of the cerebral hemispheres in which the location was known accurately and careful visual field examinations were carried out. There was a direct relationship between the presence of a visual field defect and suppression of the alpha rhythm on the corresponding side. Furthermore, complete homonymous hemianopsia was always associated with alpha suppression, whereas it was less consistently observed when the defect was partial, either in extent or in severity. Engel and his associates observed paroxysmal alpha suppression synchronous with brief homonymous scotomas in migraine,[7] and abolition of alpha activity during a transient homonymous hemianopsia following a migraine attack.[8] Likewise, when vision returns, the alpha rhythm usually accompanies it; and when it disappears, the alpha activity also does. However, we do not know whether the common influence is the visual pathway or whether the lesion affects a mechanism located in the region of the geniculocalcarine system but not functionally connected with it. This association was proposed by Williams and Reynell[35] as the result of their observation on a large number of cases with brain injuries; that is, most lesions affecting the visual radiations also impinge upon a hypothetical "source of the alpha rhythm," which they place in the parieto-occipital cortex of the convexity. They feel that these two structures, although physically close together, are not related functionally. Although light and eye opening abolish the alpha rhythm (sometimes only temporarily), other mental effort and other sense impressions can also interfere with it. Furthermore, the appearance and disappearance of alpha activity can be conditioned to a completely nonvisual stimulus.

Denial of illness in relation to the EEG was studied by Weinstein and his associates.[33,34] Their patients with denial all had bilateral EEG abnormalities; with few exceptions, strictly one-sided electrical changes were not associated with denial. This may account for the high incidence of denial of blindness in the present series, since the EEG changes, and, of course, the underlying cerebral disease, were bilateral in every instance. The widely held belief that mental changes are caused predominantly by frontal lesions was recently challenged by Battersby et al.,[10] who demonstrated that involvement of the posterior parts of the hemispheres is just as likely to produce mental and behavioral defects.

As observed by others, cerebral blindness is usually associated with disease severe enough to cause the patient's death. Persistent blindness is almost unheard of, so that if the patient lives, the blindness clears up.

The pattern of recovery is also consistent with that in previously reported cases, although none of our patients could communicate sufficiently well for detailed studies, such as those that appeared after the First World War on cases with brain injuries.[37] The recovery of central vision is typical.[25] It strengthens the theory that loss of vision from cerebral lesions is not simply a matter of cortical projections and the arrangement of fibers in the radiations, but is also a

quantitative phenomenon, in which the normally more acute central vision is the last to be destroyed and the first to recover. The pattern of recovery in Case 3, where the damage was certainly diffuse (illuminating gas poisoning), was the same as in Case 5, where the damage was localized (vascular occlusions). The manner in which recovery from homonymous hemianopsia takes place is also consistent with this view.

Testing with colored objects may bring out the purely relative character of the presence or absence of macular vision. At some stages, color perception was absent, while form and motion could be perceived adequately. If this occurred unilaterally, the macula would be "split" for color perception, whereas it would be "spared" for form and motion. This behavior also emphasizes the importance of the method of testing in describing the limits of the visual field, especially in such matters as congruity and "macular sparing." In Case 2 both homonymous fields were defective, but the left and the right were affected differently. If only motion perception and response to double simultaneous stimulation were considered, the defect would seem to be a left homonymous hemianopsia. However, when color perception and ability to localize objects were tested, the appearance was that of a right-sided field defect.

Although the criteria for cerebral blindness are well known, they are still not perfect for the study of this type of clinical material. Vision, like other forms of perception, is altered by the general condition of the nervous system, particularly the presence of mental changes. Bender [2] has demonstrated the alterations of cutaneous perception that occur in subjects with the "organic mental syndrome." Gogela and Rucker [12] found "spiral" and "tubular" visual fields in subjects with frontal tumors, that is, without involvement of the higher visual pathways. These alterations of perception are presumably caused by reduction in total cerebral function and a consequent inability to perceive two stimuli at the same time.

We can never be sure whether or not a patient with cerebral disease is blind; we can state merely that his responses to questions and observed behavior give no evidence of vision. For this reason, among others, cortical blindness is sometimes regarded as an advanced form of visual agnosia. This is unlikely, as shown by its absence in most of the recovered cases reported in the literature in which this point was mentioned and in four of the five recoveries in the present series (the fifth could not be tested satisfactorily). All four patients could recognize objects, even though there were "primary" defects in vision. One patient could name objects before she could see even light in the periphery. The ability to perceive color returned very late, even though form vision was excellent. In one patient (not in this study) with severe visual agnosia, the EEG showed diffuse slow waves, but the alpha activity was perfectly normal.

Even in cooperative subjects blindness may be hard to detect, at least in homonymous half-fields. In patients reported by Krieger and Bender,[18] the presence of some vision could not be demonstrated until they were tested with a bright light in darkness to which they had become adapted.

In three of the present cases the disorder was at some time thought to be psychogenic. Fortunately, this problem rarely arises, and the associated findings usually make the differentiation easy. The presence of occipital alpha rhythm responding to opening and closing the eyes would certainly rule out cerebral blindness, although its absence is of no significance, as it is a normal variant. A further complication is introduced by the fact that pupillary reactions to light occasionally persist in lesions of the eye and optic nerves causing apparently complete blindness. The pattern of alpha activity is, then, distinctive in the three possible conditions leading to blindness. If caused by lesions of the eye, optic nerves, or optic chiasm, alpha activity is characteristically present but is not affected by opening or closing of the eyes. In hysteria, alpha ac-

tivity is usually (but not always) present, and it disappears and reappears when the eyes are opened or closed. In cerebral blindness there is no occipital alpha activity. (Williams and Reynell's case is an exception.)

Although it is not the chief purpose of this paper to discuss the postmortem findings, it is worth mentioning that the autopsies in three cases were almost identical in that the calcarine cortex and the subjacent white matter were destroyed on both sides. Furthermore, all of the cases reported in the literature showed marked involvement of the cortex itself. It is possible that the term "cortical blindness" is a good one, although it is difficult to prove this. ("Cortical" as used here refers to the cortex and its immediate underlying white matter, as distinguished from the optic radiations in, for example, the temporal lobe.) This problem was reviewed completely by Marquis,[20] with conflicting results obtained from animal experimentation. It is apparently a fact that monkeys and all lower forms do not become completely blind after destruction of both occipital lobes.

Bramwell[3] reported a unique case in which blindness came on suddenly in the course of acute nephritis, then recovered to the extent that approximately homonymous macular half-fields remained for the rest of the patient's life. This field of vision, although tiny, was apparently normal in every respect, including color vision. (It is possible that under different conditions of testing, color vision might have been defective, as in our Case 5.) Bramwell noted specifically that "mind blindness" was not present. At autopsy, performed 26 years after the onset, the calcarine cortex on both sides was found to be destroyed, except for one occipital pole, which corresponded to the area of preserved vision. Apparently, the permanent destruction of tissue determines the permanent visual loss, whereas reversibly damaged tissue recovers in a pattern that is not solely anatomically determined.

Summary and Conclusions

Clinical and EEG observations were made in 12 cases of cerebral blindness.

The clinical features resembled those in previously reported cases.

The EEG abnormalities consisted of partial or total abolition of alpha activity, in addition to slow waves corresponding in location and severity to the nature of the underlying pathologic changes.

The pattern of recovery of the EEG in four cases is described, with the alpha activity reappearing in relation to the return of vision.

The behavior of the alpha activity in various types of cerebral lesions is compared; a relationship was found between the disappearance of alpha activity and involvement of the geniculocalcarine pathway.

Postmortem observations were made in three cases. In all of these the pathologic changes involved the calcarine cortex bilaterally.

Dr. Morris B. Bender supplied the clinical data, and Dr. Hans Strauss the EEG, in Case 12; Dr. Lewis D. Stevenson furnished all the autopsy material, including the photograph in Case 8.

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Society Transactions

CHICAGO NEUROLOGICAL SOCIETY

Irving C. Sherman, M.D., President
Oscar Sugar, M.D., Secretary
Regular Meeting, Oct. 16, 1956

Chronic Extradural Hematoma. Drs. Paul F. Nora and Paul R. Rosenbluth.

A synopsis of the main signs and symptoms of extradural hematoma is presented. The main diagnostic points are then evaluated. The pathogenesis of the disease, with special reference to the type and origin of the bleeding, is discussed. Other cases of chronic extradural hematoma are mentioned. A case report with a 21-day history of extradural hematoma is added to the literature. The frequency of extradural hematoma in head injuries is stated. Finally, the importance of the variability of the diagnostic findings is reemphasized, and the great aid that x-rays may be in establishing a diagnosis is stressed.

Discussion

Dr. Harold C. Voris: This is a very good and important paper. So-called chronic extradural hematoma, or at least extradural hematoma not recognized for some time after injury, is, I believe, more important than one would suppose from the literature. I reported a series of cases some 10 years ago which fell into this group.

I think the authors have described the mechanism pretty well. I would only emphasize that if rupture of the communications between diploic vessels and dural vessels—and I think that is the initial hemorrhage—occurs, this initial hemorrhage separates the dura from the bone over a small area. Many of you have seen these bleeding points when an osteoplastic craniotomy is performed. I am sure the dura is separated from the bone and these bleeding points exist. The venous pressure is low, so that the bleeding from any one point is not great but is progressive, and small progressive hemorrhages continue until the hematoma is recognized. It is a mistake to think that because a patient was injured two or three weeks ago he cannot have an extradural hemorrhage.

Dr. Paul R. Rosenbluth, I appreciate Dr. Voris' discussion. His paper dealing with extradural bleeding from the venous sinuses was a great help to us. This is a rare surgical finding, which one should keep in mind. It should be emphasized that skull x-rays are helpful here, although usually proscribed in acute head injuries. In chronic extradural hematoma the x-ray may reveal fracture lines across the vascular sinuses and pineal shift.

Skeletal Muscle from Muscular Dystrophy Patients Cultured in Vitro. Dr. Ruth S. Geiger.

In the present work an attempt was made to determine any inherent characteristics of skeletal muscle cells from patients with progressive muscular dystrophy (diagnosed by Dr. J. S. Garvin). The tissue culture technique makes feasible the maintenance of muscle tissue of various origins under identical environmental conditions and affords the possibility of observing the behavior, growth, and regeneration of cells away from the influence of the organism. Studies were carried out on skeletal muscle biopsy specimens from seven patients suffering from pseudohypertrophic muscular dystrophy and from one patient with dystrophica myotonica. The results showed strikingly different regenerative properties in the skeletal muscle from patients with progressive muscular dystrophies as compared with normal human skeletal muscle.

The dystrophic muscle cells had a shorter dormancy period than the normal in fresh explants, appeared more granular, and did not develop cross striations. They showed little or no spontaneous contraction (except for the dystrophica myotonica) when observed with time-lapse microphotography. After about 3-5 weeks in culture, or 7-10 days after being subcultured, the dystrophic cells undergo marked hypertrophy, usually coincident with the appearance of exaggerated longitudinal striations. These cells may reach sizes of 1 to 3 mm in length and 100μ to 400μ in diameter and contain as many as 60 to 80 nuclei produced by amitotic division, as observed with time-lapse microphotography. Numerous droplets aligned between the longitudinal striations appear in areas of sarcoplasm. This process of abortive regeneration extended over a period of three to four weeks in subculture. These giant cells finally broke up into fragments, which rapidly degenerated, despite the presence of nuclei in the fragments. The pseudohypertrophic dystrophy muscle could be successfully subcultured through one passage only.

Under identical conditions, normal skeletal muscle cells usually do not exceed 200μ-300μ in

length and generally contain a maximum of five or six nuclei. They undergo periodic budding, develop cross striations, and show spontaneous contractility. Normal skeletal muscle cells can be maintained indefinitely in culture. In our laboratory they have been maintained for one and a half years, through 16 successive subcultures. Both mitosis and amitosis have been observed in normal skeletal muscle cells.

Diagnostic Value of Muscle Tissue Culture. Dr. John S. Garvin, M.D.

Utilizing the method of muscle tissue culture, as previously described by Dr. Geiger, the growth patterns were correlated with the clinical history and diagnoses. The history and clinical findings were presented, along with the tissue culture results. Three patients with the diagnosis of muscular dystrophy with pseudohypertrophy showed essentially the same pattern regardless of the stage of the disease. The muscle cells had a shorter latent period than the normal, had many nuclei (50-60), were more granular, developed no cross striations, and were larger than normal. One patient with dystrophia myotonica showed a similar pattern except that the cells had more fat granules and also showed spontaneous contractions. One patient whose clinical diagnosis is in doubt, whether she had thyrotoxic myopathy or polymyositis, had a pattern different from the dystrophic cells and from normal muscle. The latency period was extremely short, but the cells showed characteristics of normal muscle. The cells did not subculture like the normal and degenerated quickly at about the third week. One patient whose condition had been diagnosed as muscular dystrophy showed a normal pattern of tissue growth with cross striations. This patient subsequently developed a Babinski sign and involvement of the posterior columns, and a definitive diagnosis of spinocerebellar ataxia was made.

Muscle tissue culture is a method by which a definite and reproducible pattern of growth and type of cell are seen. Normal muscle and atrophic muscle from neurologic causes produce the same picture. The growth and appearance of dystrophic cells is markedly different, thus enabling us to use tissue culture as an early diagnostic confirmatory test. Other diseases of the muscle which show different patterns from both the normal and the dystrophic cells are being investigated. Why the difference occurs gives rise to many theories, some of which are in the process of investigation.

Discussion

On Papers by Drs. Geiger and Garvin

Dr. Reuben M. Strong: If I understood Dr. Garvin correctly, he implied that normal muscle had many nuclei.

Dr. John S. Garvin: What I meant was that in normal muscle nuclei are seen, but not in as great numbers as 50-60, which are found in dystrophic cells.

Dr. L. M. Eaton, Rochester, Minn.: I was particularly interested in the work we have heard reported on tissue culture. I had hoped that it might have progressed far enough to settle the problem as to whether or not the defect in muscular dystrophy is primarily in the muscle fiber itself or is secondary to some extramuscular biochemical abnormality. Since muscle removed from the patient with the Duchenne type of dystrophy ("pseudohypertrophic") grew abnormally in tissue culture, one might have suspected that the defect was inherent in the muscle fiber itself. However, since muscle fibers from the patient who had an acquired myopathy (the case of so-called "thyrotoxic myopathy") also grew abnormally in tissue culture, that assumption is untenable. In any event, the work is of great interest, and I trust that in time it will help elucidate the fundamental problems related to the myopathies.

Dr. Ruth S. Geiger: There are several reasons for supposing that the differences observed in the regenerative pattern of skeletal muscle cells from patients with progressive muscular dystrophies are inherent in the muscle cells. Away from any influence of the organism and under identical conditions (feeding solution, etc.) these cells develop quite differently from normal ones. The rapid regeneration of nuclei with subsequent degeneration of the cell is characteristic of this disease, and its mechanism is being investigated. The considerably shorter dormancy period of these cells further indicates a fundamental difference. There comes to mind the fact that tumor cells generally exhibit shorter dormancy periods, as does tissue treated with low doses of x-rays. In my experience thus far in tissue culture, skeletal muscle cells from cases of secondary muscular atrophies behave in a manner similar to normal skeletal muscle.

Is There a Pyramidal Tract? Dr. Paul C. Bucy

Since Ferrier demonstrated the electrical excitability of the precentral gyrus in 1873 and Betz described the gigantic cells of that gyrus, the control of the activity of the skeletal musculature by the Betz cells and their axones has been generally accepted. This view was strongly reinforced in 1909, when Gordon Holmes and Page May apparently demonstrated that the pyramidal tract (which may be defined as those fibers which are found descending in the pyramids on the ventral surface of the medulla oblongata) arose exclusively from the Betz cells in the precentral gyrus. Furthermore, it was also generally accepted that destruction of the pyramidal tract gave rise to a spastic paralysis without atrophy, with hyperactive

tendon reflexes, an abolition of the abdominal reflexes, and the possibility of eliciting the sign of Babinski—the "pyramidal syndrome."

Doubt began to be cast upon this simple explanation of the neural motor mechanism by Fulton and his co-workers when they showed that lesions of the precentral gyrus could give rise to paralysis without striking spasticity, and by Marion Hines when she demonstrated that spasticity was in considerable measure dependent upon destruction of the "strip" (later designated as Area 4s by Dusser de Barenne, McCulloch, and their associates). Further evidence was developed by Bucy and Fulton. They demonstrated that extirpation of the precentral gyrus bilaterally (thus presumably destroying the pyramidal tracts) not only did not completely paralyze the animal but left one that could sit, stand, walk, run, and climb the walls of its cage. Total paralysis was produced only when both Area 4 and Area 6 were destroyed bilaterally. Since then Kennard has shown that even such an extensive extirpation does not result in a complete paralysis if carried out in infant monkeys, and Travis and Woolsey have demonstrated that if the extirpations are made piecemeal over many months and if the monkey is given the most painstaking of care, the entire cerebral cortex can be removed and a considerable degree of crude motor function retained. Tower confirmed Fulton's opinion that the pyramidal tract does not inhibit postural reflexes when she sectioned the entire pyramidal tract on the ventral surface of the medulla oblongata without producing spasticity, or a complete paralysis.

In 1937 Häggqvist raised doubts as to the unity and origin of the pyramidal tract. He found that after extirpation of the precentral gyrus in the monkey much of the pyramidal tract remains intact. Since then Lassek, Levin and Bradford, and others have extended our knowledge, or pointed out our ignorance, regarding the structure of the pyramidal tract. At the present time it appears that approximately 3% or 4% of the pyramidal tract arises from the Betz cells, another 24% to 37% arises from other cells in the precentral gyrus, and approximately 20% arises from the cortex of the parietal lobe. Thus the origin of some 50% or 60% of these fibers is known. Whereas we not only do not know where the other 40% to 50% come from, we are not even certain that they are of cortical origin.

No evidence demonstrated as true for laboratory animals is necessarily true for man. It can only be accepted for man after adequate confirmation. It has been shown that extirpation of the precentral region (Areas 4 and 6) from one human cerebral hemisphere does not produce a total paralysis of the contralateral extremities (Bucy). But it is thought that the remaining function is probably due to ipsilateral innervation. Putnam sectioned the pyramidal tract in the upper cervical spinal cord and produced far less paralysis than was anticipated. Because it was impossible to be sure of the completeness of the section, this observation may not have received the attention it deserved. More recently Walker has sectioned variable amounts of the lateral parts of the cerebral peduncles in nine patients. Two of these developed severe hemiplegias; one has a moderate hemiparesis, but six have no, or only slight, paralysis. Levin has shown that the corticospinal fibers arising from the precentral gyrus occupy the central part of the cerebral peduncle. The medial quarter is occupied by frontopontine fibers, while in the lateral quarter are found parietopontine fibers. Meyers demonstrated that section of the medial quarter of the peduncle (frontopontine fibers) neither abolished abnormal involuntary movements nor permanently affected the motor activities of the patients.

Three patients are described here. In the first, a patient with severe unilateral (right) Parkinsonism, the lateral quarter of the left cerebral peduncle (parietopontine fibers) was sectioned without abolishing the tremor, paralyzing the patient, or altering his reflex status. In the second patient, who suffered from severe left hemiballismus for over 30 years, most of the central half of the right cerebral peduncle was sectioned. The movements have been reduced to approximately 25% of their preoperative intensity, but the patient is not paralyzed. She walks well and has voluntary movements at all joints in her left extremities, including independent movement of individual fingers. There is no spasticity, and the tendon reflexes are increased about the same as they were prior to the operation. But the sign of Babinski, which was not present before, can now be elicited. In the third patient, a 33-year-old victim of unusually severe multiple sclerosis, there was bilateral impairment of vision, incapacitating paraplegia in flexion, incontinence of urine, and violent ballismic movements of the arms, much greater on the left. All of the central portion of her right cerebral peduncle was sectioned, leaving only the medial one-sixth and the lateral one-fourth intact. The abnormal involuntary movements of her left upper extremity are greatly reduced. The hand lies quietly at rest, and involuntary movements of greatly reduced intensity appear only when the arm is moved intentionally. She, too, has voluntary movements at all joints in the left upper extremity and can move each finger independently.

It is obvious that the pyramidal tract is not a single entity and that the origin, course, and termination of many of the fibers of the pyramids are unknown. It is equally obvious that the function of the pyramidal tract is most imperfectly

understood. The pyramidal syndrome of spastic paralysis with hyperactive tendon reflexes, absence of abdominal reflexes, and the sign of Babinski is not the result of destruction of the corticospinal fibers descending from the precentral gyrus.

We must be careful not to make the mistake of equating deficit with function. Merely that little or no paralysis appears when the corticospinal fibers from the precentral gyrus are destroyed does not mean that they are devoid of motor function.

Unfortunately, at this time we are not in position to define accurately and completely the neural mechanism responsible for the activity of the skeletal musculature, either as to structure or as to function. We must discard such inaccurate concepts as the "pyramidal tract" and the "pyramidal syndrome." (And certainly if there is no pyramidal tract, there can hardly be an extrapyramidal tract or system). We must resume our task and continue our investigations both on animals and on man until the facts of both structure and function have been demonstrated.

Discussion

Dr. H. Russell Meyers, Iowa City: What Dr. Bucy has had to say about the dubious character of the pyramidal tract leads me to make some general remarks about medical education in general and neurological teaching in particular. For many years, now, a great many medical students have been learning "facts" concerning the anatomy, physiology, pathology, and clinical aspects of the "pyramidal system" that simply are not so. There are many other aspects of neurology concerning which much the same might be said. A question arises as to why we should be so long in emending such teaching and learning. It would appear that for a good part of our education high premiums are placed on the ability to give answers, right or wrong, and virtually none on the very important process of asking meaningful questions. It is all too easy, under the cloak of scholarliness, to reiterate notions that have become well entrenched in the literature. It appears, as Alan Gregg once put it, that we are far less interested in finding out what our students know than we are in assuring ourselves that they know what we know.

Dr. Bucy has indicated that up to the present one of the links in our chain of evidence has been missing. This link bears reference to an autopsy demonstration from the human showing conclusively that the "pyramidal tract" has been sectioned in the crus. I am in a position to report that we now have two autopsy cases of patients who died following surgical section of the crus for choreoathetosis associated with cerebral palsy. These demonstrate clearly that the surgical incision was made where it was intended to be. The incision occupies the intermediate three-fifths of the crus, in which the pyramidal tract is conventionally pictured in our textbooks, and, further, extends very slightly beyond this portion of the crus, both medially and laterally. Thus, we are now furnished with an additional and necessary piece of information bearing on tonight's thesis.

I should like to confirm what Dr. Bucy has been emphasizing by synopsizing a paper entitled "The Extrapyramidal System: An Inquiry into the Validity of the Concept," which I published in *Neurology* (3:627, 1953). In this paper, the approach is made by a different route, namely, a study of the "extrapyramidal system," but the conclusion is the same—that the concept of a pyramidal tract and pyramidal system (upon the substantial character of which the notion of an extrapyramidal system ultimately revolves) is singularly tenuous and operationally insubstantial. Hence, to make use of these terms for purposes of clinical study, teaching, and research is equivalent to writing a check for which there is no money in the bank.

The extrapyramidal system and, for that matter, the pyramidal system are not "demonstrated facts," as many students of neurology appear to believe, but man-made concepts, that is, verbal maps, intended to describe and account for certain empirically observable aspects of the structure and function of the nervous system. There is nothing sacred or inevitable about them; they are not, and never can be, more valid than the organismic events they are intended to represent.

Profitable discussion of our subject requires clear recognition of the historical circumstance that the concept of the extrapyramidal system was antedated by, and throughout the years since its inception has been conditioned upon, the concept of the pyramidal system. For this reason, the validity of the extrapyramidal concept depends in considerable measure upon how convincing a case can be made out for the pyramidal. This much follows from the contention that the extrapyramidal system consists of "all efferent mechanisms apart from the pyramidal tract which have to do with motor activity." As a neurologic map, the definition clearly depicts the circumstance of a dichotomy, in view of which it becomes important to ascertain whether a phenomenal dichotomy is discoverable in the territory for which the map stands.

Suffice it to say that by the use of Boolian algebra and modern symbolic logic, the dichotomy can readily be shown to be a figment of imagination. There is no anatomic, physiologic, pathologic, or phylogenetic reason for regarding the pyramidal system as "an entity." Moreover, the concept that the pyramidal system mediates "voluntary" movements and fine, discrete, skilled acts is vitiated on

at least three grounds: 1. We posses no criteria by which voluntary acts can operationally be distinguished from involuntary. 2. Section of the nervous system at various levels considered to represent the "pyramidal system"—cortical, capsular, peduncular, medullary, and spinal—proves conclusively that "voluntary" movement, as loosely used in a clinical sense, is not abolished, but merely impaired. 3. While damage to the portions of the nervous system at the levels mentioned results in dyspraxia, damage to other parts of the nervous system not considered "pyramidal," e. g., the premotor cortex, likewise results in dyspraxia.

A similar careful analysis reveals there is little or no substance for establishing an "extrapyramidal system." On logical grounds alone, we would be entitled to suspect the proposition that everything which is not pyramidal must somehow constitute a system the components of which belong together in some peculiar way not discernible as between pyramidal and extrapyramidal elements.

The pyramidal tract, from which the name of the so-called neural system has been derived, obviously includes a number of neural elements which cannot properly be considered parts of the pyramidal system. For this, and other reasons, the pyramidal system appears to be an uncertain concept. By the same token, the extrapyramidal system, which by definition, depends for its claim to anatomic and physiologic discreteness upon being nonpyramidal, appears similarly uncertain, if not largely fanciful. Of even greater significance is the fact that clinicopathologic and experimental findings cannot readily be reconciled with current anatomic and functional concepts of the so-called pyramidal and extrapyramidal motor systems.

DR. BENJAMIN BOSHES: Last spring I took part in a symposium on the pyramidal tract. Dr. Bucy had been invited and was not able to participate in that symposium; therefore, I was happy to have his clear description. As long as the pillars of the neurologic temple are coming down, I should like to pull down a few remaining ones. I should like to read from my paper a small section on reflexes, particularly the Babinski sign, because the British contributed to that confusion.

First, as to the area of pathologic reflexes in the foot that are supposed to pertain to the pyramidal tract: The Babinski sign was described over 50 years ago, and we are asking this question about the sign now. In 1955 Nathan and Smith examined the Babinski sign and reported in a recent issue of *Brain* that after examination of patients in whom various types of chordotomy were performed to alleviate the pain of malignant disease, lesions of the lateral quadrants of the cord resection may or may not cause the Babinski sign; (2) no conclusion can be drawn as to the tract involved when the Babinski sign is positive; (3) the Babinski sign may be found when the pyramidal tract appears normal; (4) lesion of the anterior half of the cord may be accompanied by a Babinski sign; (5) identical lesions on two sides of the cord may give a Babinski sign on one side. They conclude that to regard the Babinski sign as a reflex is a simple conception of neurophysiology. To test this, I asked Dr. Kesert, at the Veterans' Administration Hospital, Hines, Ill., to test the reflexes on 100 spinal cord patients to see in how many the Babinski sign was present. In this group of 100, all in good condition, we had 52 verified complete lesions and 48 incomplete, but very severe, lesions. Of 100 patients the Babinski sign was found in 15. Of the 52 with complete lesions, only 11 had the Babinski sign. Analysis of the responses of these patients shows that 12% had dorsiflexion of the big toe, 6% had fanning, 33% had the Babinski sign plus a flexor synergy, and 21% had straight withdrawal. In our own material at Hines, it is apparent that the Babinski sign is not directly related to the disturbance in the pyramidal tract. Lassek studied anatomically lesions after massive paralyses. Of this series, 57.5% had no lesions involving the pyramidal tract. He has a large series of congenital cases in which there was paralysis and the pyramidal tract was intact.

PHILADELPHIA NEUROLOGICAL SOCIETY

Ernest A. Spiegel, M.D., Presiding
Regular Meeting, Dec. 14, 1956

Present Status of Radioisotopes in Neurology and Neurosurgery. Dr. B. Selverstone (by invitation).

At both the fundamental and the clinical level, radioactive isotopes have added useful new techniques to neurology and neurosurgery. Tracer studies have permitted an analysis of exchanges of ionic and other substances among blood, brain, and cerebrospinal fluid. They have as yet cast little light upon the so-called "blood-brain barrier" except to indicate that it is an even more complex phenomenon than has previously been thought. The behavior of trace elements may be studied, such as, for example, copper in hepatolenticular degeneration (Wilson's disease), but it must be remembered that such investigations complement, rather than replace, the more tedious determinations of metabolic balance. The differences between gliomas and the normal brain may be advantageously studied by means of the tracer technique, and results of such investigations with P^{32}, K^{42}, and Na^{24} will be presented.

Localization of brain tumors with radioactive isotopes has aroused considerable interest. It comprises two phases—localization at operation by means of beta-ray-emitting substances, and preoperative localization with gamma rays. Both techniques depend upon the differential concentration of a tagged substance in the tumor. Relatively small differentials have been obtained using labeled dyestuffs and albumin, which depend for their usefulness upon an altered vascular permeability in the neoplasm. Substances such as K^{42}, whose concentration in the tumor depends upon metabolic properties of the neoplasm, reach much higher differential concentrations. The physical properties of the isotope may impose limitations or permit refinements of technique, for it is difficult to collimate the more energetic gamma rays, such as those of K^{42}. Pulse height analysis and the positron techniques may help with some of the physical problems of tumor localization.

Discussion

Dr. M. Scott: Have you done experiments with the choroid plexus removed?

Dr. B. Selverstone: No. Our studies have been on humans.

Dr. G. M. Austin: I should like to have seen more detailed evidence, such as scatter charts, rather than conclusions and smooth curves.

Dr. B. Selverstone: I have the material but did not show it because of lack of time. I am very critical of our work and calculate errors carefully.

Dr. G. M. Austin: Have you done studies on patients with obstructive hydrocephalus?

Dr. B. Selverstone: No. We have studied a case with a high cervical block in which exchange of spinal fluid constituents below the block was the same as in normal studies.

Dr. H. T. Wycis: Is it not true that the size of the spinal fluid samples affects the results and tends to alter the constituents?

Dr. B. Selverstone: We took 0.2 cc. samples, which were as small as possible, in order to minimize this source of error.

Dr. M. Scott: Can you rely on this method to tell when the needle is outside the limits of the tumor?

Dr. B. Selverstone: Not always. There are two fallacies in this method. If the counterneedle is placed on the surface of a portion of the brain remaining after a resection has been performed, e. g., frontal lobectomy, the high count is unreliable, since the radiation is reaching the counter through air from all directions. The second fallacy is that one cell of tumor considerably separate from the main body of the tumor will give a count as much as 20% higher than normal tissue. The tumor itself may give counts 20 times normal. The maximal limit of normal is a count of radiation five times the normal tissue radiation. This method of localization is not reliable for delineating the limits of a tumor and is best used to find a small hidden tumor.

Dr. G. M. Austin: How much P^{32} is used as a testing dose?

Dr. B. Selverstone: One millicurie; however, as little as 0.25 mc. may be used.

Dr. A. Silverstein: Have you had any instance in which all other studies failed to reveal a tumor that was then disclosed by this method?

Dr. B. Selverstone: I do not operate in the presence of normal studies and therefore have not attempted to locate a previously undiagnosed tumor.

Dr. A. Silverstein: Was there any instance in which this procedure of study made any real difference in the outcome of the case?

Dr. B. Selverstone: No, as far as the decision to operate and survival is concerned; but it helps

to find small tumors in a shorter time. It also helps to decrease the amount of manipulation and exploration and therefore tends to minimize the amount of brain swelling postoperatively. The procedure takes only a couple of minutes and often saves much time otherwise caused by manipulation and exploration.

DR. M. SCOTT: Have you studied cord neoplasms in this manner?

DR. B. SELVERSTONE: No. I would not put a 2 mm. probe into the cord. Maybe, after we have probes that are 0.7 or 0.8 mm. in diameter, we will use it on the cord.

DR. H. T. WYCIS: Has the use of this technique resulted in the decision to operate or not?

DR. B. SELVERSTONE: Only in an emergency, when time did not permit an air study and the operation was necessary on clinical grounds. We

DR. E. A. SPIEGEL: Is there any difference definitely.

in the uptake of the labeled isotope from gray have then used this method to locate the tumor and white matter, infarcted area, and brain abscess?

DR. B. SELVERSTONE: Uptake of P^{32} in gray matter is from 50% to three times that in white matter. There is not increase of uptake in infarcted areas or in areas of destruction. The wall of an abscess does have a high uptake, as high as tumor.

DR. H. T. WYCIS: I am surprised that the protein-fraction findings were not more striking. We found this fraction to be very significant in enzyme studies on brain tissue.

DR. B. SELVERSTONE: It is significant as far as tumor versus normal tissue is concerned, but is not as significant as the phospholysed fraction.

DR. E. A. SPIEGEL: How much difference is there between the determinations of intracellular and of extracellular ions in edematous tissue?

DR. B. SELVERSTONE: We have no answers on that problem yet.

DR. N. S. SCHLEZINGER: Have you any material concerning these studies on tumor tissue cultures?

DR. B. SELVERSTONE: We have no experience with tissue cultures. This technique is too gross for that.

DR. H. T. WYCIS: Can you gain any information concerning posterior-fossa tumors with K^{42}?

DR. B. SELVERSTONE: K^{42} is worthless in attempting to localize posterior fossa tumors.

DR. C. RUPP: Is there any way of localizing brain-stem tumors by radioactivity studies?

DR. B. SELVERSTONE: Brain-stem tumors cannot be localized externally; they can be only by laying the counter on the side of the stem at operation, but this is usually unnecessary, since the tumor can be well localized by clinical means.

DR. E. A. SPIEGEL: Can these materials be used therapeutically?

DR. B. SELVERSTONE: K^{42} cannot be used therapeutically by injection into the blood, since its uptake is as great by the liver, bone marrow, and spleen as by the brain tumor.

DR. E. A. SPIEGEL: Could K^{42} be used therapeutically by direct infiltration of the tumor?

DR. SELVERSTONE: Yes, it would be a valid method, as is done in other tumors, but no better than, or different from, other methods of irradiation therapy already in use.

Renografin as a New Contrast Medium for Cerebral Arteriography: Animal Experiments.

DR. DAVID LA FIA AND DR. RUDOLPH JAEGER.

Renografin is one of the new contrast agents for cerebral angiography. It is a triiode compound, like acetrizoate (Urokon), diatrizoate (Hypaque) and diprotrizoate (Miokon). It was tested on dogs for toxicity, irritation of the brain cortex and soft tissues, and radiopacity. Toxicity was measured by death of the animal, convulsions, or breakdown of the blood-brain barrier. It was compared with Thorotrast, idiodopyracet (Diodrast), acetrizoate, diatrizoate, and diprotrizoate. Twenty dog experiments revealed that Renografin was (1) relatively nontoxic, causing convulsions and death in one animal in amounts of 50 cc. (in nine animals it did not cause death until amounts greater than 110 cc. were used), (2) nonirritating to the soft tissues and the brain cortex, and (3) productive of good arteriograms, with contrasts as sharp as those with Thorotrast.

Discussion

DR. RUDOLPH JAEGER: This material still has the disadvantages that other soluble iodides have. It is less irritating than inorganic iodides. Insoluble colloidal suspensions are safe, since they do not enter brain tissue. There are no serious delayed reactions from these organic iodides, and we need not fear them, e. g., Thorotrast. No malignancy results from use of Thorotrast. We would like to get away from soluble iodides.

DR. M. SCOTT: Thanks to Dr. La Fia for this work on animals first, before using it on humans. This is the right approach.

DR. A. K. OLSEN: We have used Renografin on 12 patients and obtained good contrast, but saw no other difference and there were no unfavorable effects.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Psychiatry and Psychopathology

RH CHILD: DEAF OR 'APHASIC'?: 4. VARIATIONS IN THE AUDITORY DISORDERS OF THE RH CHILD. J. ROSEN, J. Speech & Hearing Disorders 21:418 (Dec.) 1956.

Thirty-three children were seen at San Francisco Hearing and Speech Center with clear-cut diagnoses of erythroblastosis fetalis and kernicterus, 16 boys and 17 girls, with an age range of 6 months to 14 years and a mean age of 7 years. Of the 33 all previously diagnosed as deaf or hard of hearing, 11 were found to have normal hearing. Seven children responded at levels of 15-20 db. throughout the range of frequencies from 250 to 4000 cps. Various levels of auditory sensitivity, from 25-60 db., were established for 12 of the children. There were only three cases in which audiometric results and observations suggested the existence of an actual hearing loss. One of these children responded to high-frequency tones in a manner which strongly suggested the presence of recruitment. "Fluctuations," so frequently noted in the Rh child's apparent ability to hear, were not confined to hearing alone. Visual and tactile stimuli often elicit inconsistent responses. Auditory disorders in these children take a variety of forms. School placement is a most complex problem.

PALMER, Wichita, Kan.

RH CHILD: DEAF OR 'APHASIC'?: 5. SOME PSYCHOLOGICAL CONSIDERATIONS OF THE RH CHILD, J. Speech & Hearing Disorders 21:423 (Dec.) 1956.

Rh children seem to be more like aphasic children than children with deafness. Rh children should be viewed primarily from the point of view of psychology of brain injury rather than from the point of view of psychology of deafness.

PALMER, Wichita, Kan.

CORRELATION BETWEEN TWO MEASURES OF THE SEVERITY OF STUTTERING. D. SHERMAN and W. D. TROTTER, J. Speech & Hearing Disorders 21:426 (Dec.) 1956.

The data for five successive readings of a 500-word passage by each of 20 stutterers were analyzed. The frequency and mean rate of severity of individual moments of stuttering are significantly and positively correlated. The strength of relationship was not varied over the course of five successive readings. The relationship is not strong enough that one measure can be useful in predicting the other. A complete evaluation of severity of audible characteristics of stuttering should probably take into account both frequency and severity of individual moments of stuttering.

PALMER, Wichita, Kan.

MMPI PROFILES OF STUTTERERS' PARENTS: A FOLLOW-UP STUDY. L. D. GOODSTEIN, J. Speech & Hearing Disorders 21:430 (Dec.) 1956.

The author cross validated with a typical speech-clinic group of children, approximately 10 years of age, the findings of a previous study that had found no major differences in the Minnesota Multiphasic Personality Inventory profiles of a group of 100 parents of stutterers and 100 parents of nonstutterers. Case records of 50 stuttering children and their parents were drawn from the files of the State University of Iowa Speech Clinic, and the 100 profiles were compared with the results of the previous study. Only three significant mean differences were found, and comparisons of the high-point codes of the parents in the follow-up study and of the two original groups revealed no significant differences. The study is interpreted as confirming the conclusions of the prior study that the etiology of stuttering is not related to severe psychopathology on the part of stutterers' parents.

PALMER, Wichita, Kan.

ARTICULATION OF A GROUP OF CHILDREN WITH CLEFT LIPS AND PALATES. D. C. SPRIESTERSBACH, F. L. DARLEY, and V. ROUSE, J. Speech & Hearing Disorders 21:436 (Dec.) 1956.

The speech of 25 Caucasian children between the ages of 3 and 8.1 years with cleft palate and/or cleft lip were analyzed on the Templin Diagnostic Articulation Test. There was little difficulty in articulation of vowels and diphthongs; consonants misarticulated more than 60% of the time were as follows: z, voiceless th, s, tsh, zh, dzh, voiced th, sh, and t. This group of cleft-palate children seemed to be generally retarded in articulation, had significantly less difficulty with voiced consonants than voiceless consonants, had less difficulty on nasal consonants, but had the greatest difficulty with fricative consonants. Omission-type errors were observed most frequently, followed by substitutions and distortions. This group of children had significantly less difficulty in producing consonants correctly when they appeared as singles than as elements of blends. These cleft-palate children were generally inconsistent in their misarticulation.

PALMER, Wichita, Kan.

SHORT TEST FOR USE WITH CEREBRAL PALSY CHILDREN. O. C. IRWIN, J. Speech & Hearing Disorders 21:446 (Dec.) 1956.

A short test of five consonants incorporated in a list of 15 words was given to 96 cerebral palsy children from 4 to 16 years of age. Consonants were p, b, m, d, and t. The study concerned an analysis of the internal relationships among a selection of these consonants. Four criteria were considered: reliability, difficulty of items, discriminating power, and uniqueness. Coefficient of reliability for the verbal part of the test was 0.91, and for the picture test, 0.92. Difficulties of items ranged from 33% to 88%. Discriminating power of items was high, the median coefficient being 0.75, whereas uniqueness of the items had a median coefficient of 0.47. The words used were ball, bed, rabbit, tub, cup, ice cream, milk, pig, hat, mama, kitten, dog, candy, table, and apple, presented in the form of pictures, to which the children were instructed to respond when spoken by the experimenter with the request that the children repeat the word.

PALMER, Wichita, Kan.

LANGUAGE INVESTIGATION OF CHILDREN SUFFERING FROM FAMILIAL DYSAUTONOMIA. K. DE HIRSCH and J. J. JANSKY, J. Speech & Hearing Disorders 21:450 (Dec.) 1956.

Twelve children suffering from familial dysautonomia were studied relative to difficulties with gross and finer motor control and associated difficulties with movement and control of articulatory structures. Breathing, swallowing, chewing, and sucking were difficult. The voices of these children were deviating: Quality was nasalized, pitch monotonous; there was poor control of loudness and a tendency to fading. Auditory memory span was short. There were fluctuations in rate. Articulation was inferior to what one would expect in the general population. Difficulty with story telling was relatively frequent. Categorical behavior seemed to be poor. The difficulty resembled speech manifestations in cases of congenital suprabulbar agenesis, as well as in bilateral and extrapyramidal lesions.

PALMER, Wichita, Kan.

WHAT MAKES AN EFFECTIVE PUBLIC SCHOOL SPEECH THERAPIST? M. H. POWERS, J. Speech & Hearing Disorders 21:461 (Dec.) 1956.

The author presents an outline of the complex characteristics, skills, and attitudes that a public school speech therapist should possess.

PALMER, Wichita, Kan.

PSYCHOLINGUISTIC STUDY OF APHASIA: A REVISION OF THE CONCEPT OF ANOMIA. J. M. WEPMAN, R. D. BOCK, L. V. JONES, and D. VAN PELT, J. Speech & Hearing Disorders 21:468 (Dec.) 1956.

An aphasic adult with anomia was compared on the basis of a normal model of speech with a normal subject. It seemed possible to hypothesize that anomia may be characterized by the loss of all but the most general (and hence most frequent) words in the language, and that therefore such a patient has suffered disruption of voluntary control of those relatively infrequent words which carry essential information but has retained more or less automatic use of highly frequent words.

PALMER, Wichita, Kan.

Teacher Judgment of Hearing Loss in Children. M. L. Geyer and A. Yankauer, J. Speech & Hearing Disorders 21:482 (Dec.) 1956.

Teacher-judgments of hearing loss based upon a check list of symptoms and signs were obtained on 1053 first- and second-grade children in seven schools. All children were screened for hearing loss by individual pure-tone sweep-check testing. Children failing this screening test were threshold-tested and seen by an otologist. Teachers "oversuspected" children to an appreciable extent and failed to suspect 62% of children with a hearing loss. However, the incidence of hearing loss was twice as great in the "teacher-suspected" group as in the "unsuspected" group. No relationship was found between the effectiveness of teacher selection and severity of hearing loss at speech frequencies (except when moderately severe), sex of child, size of class, nature of symptoms or signs, or individual teachers and schools.

Palmer, Wichita, Kan.

Testing the Hearing of the Mentally Retarded. B. B. Schlanger and R. H. Gottsleben, J. Speech & Hearing Disorders 21:487 (Dec.) 1956.

Pure-tone audiometric tests were administered to 498 mentally retarded subjects at the Training School at Vineland, N. J. Of these, 35% had normal hearing, 14% only slight deviation, and 28% moderate losses; 6% were hard of hearing, and 1% were deaf. Seventeen per cent of the population was nontestable, with a mental age below 5 years, personality disturbances, and social quotients below 40. Four-fifths of this group were of either organic or mongoloid etiology. The authors discussed the problems of testing a group of this type. A routine hearing examination of all retarded children should be carried out.

Palmer, Wichita, Kan.

Meninges and Blood Vessels

An Outbreak of Aseptic Meningitis of Virus Origin. D. G. Garnett, A. Burlingham, and D. van Zwanenberg, Lancet 1:500 (March 9) 1957.

The authors report an illness which occurred in Suffolk, England, in September, 1955, which had not been observed previously. The predominant signs and symptoms were fever, headache, nausea and vomiting, pain in the neck and shoulders, flushed face, photophobia, and, in about 25% of the cases (mostly children), a macular rash, often rubelliform in type. Recovery was usually rapid and always complete, without paralysis or other residual effects. A large number of cells were present in the spinal fluid of the patients admitted to the hospital; these were predominantly polymorphonuclear leukocytes in the early stage and lymphocytes later. The total protein in the 11 cases was never found to exceed 60 mg. per 100 cc., and in 6 out of the 11 it did not exceed 30 mg. per 100 cc. Headache and vomiting were considerably relieved by lumbar puncture.

Strains of virus immunologically related to the Echo-9 type of enteric virus were isolated from the cerebrospinal fluid of five patients, from the stools of six, and from the throat washings of four.

Yaskin, Camden, N. J.

Meningitis of Virus Origin. C. E. Rotem, Lancet 1:502 (March 9) 1957.

Rotem reports a review of 100 patients suffering from an aseptic meningitis who were studied after admission to the Leicester Isolation Hospital. The disease, apparently widespread all over England, was most prevalent in the Midlands. These cases were all admitted and studied between July 4 and Nov. 23, 1956. The main clinical features of the disease were acute onset, headache, pyrexia, vomiting, neck and back rigidity, and, occasionally, a rubelliform rash and photophobia. A predominantly lymphocytic pleocytosis was found in the cerebrospinal fluid of most patients. Adenopathy was not a feature of the disease. All patients recovered without specific treatment, and with no serious sequelae. A cytopathogenic virus related to Echo virus Type 9 was isolated from feces, cerebrospinal fluid, and throat swabs in several cases. It is concluded that this essentially benign disease is probably not identical with lymphyocytic meningoencephalitis but shows clinical similarity with cases described by Karzon and by Dodd.

Yaskin, Camden, N. J.

Diseases of the Brain

THE SYNDROME OF PSEUDO-PSEUDOHYPOPARATHYROIDISM. S. WALLACH, E. ENGLERT JR., and H. BROWN, A. M. A. Arch. Int. Med. 98:517 (Oct.) 1956.

Genuine hypoparathyroidism is a state wherein defective parathyroid function results in excessive renal phosphate reabsorption, consequent hypocalcemia, neurological symptoms, consisting of tetany, convulsive seizures, and basal ganglia calcification, and skeletal changes. Under certain circumstances a similar syndrome develops when there is inadequate renal response to normally functioning parathyroid glands. The latter state of end-organ refractoriness is termed pseudohypoparathyroidism. The term pseudo-pseudohypoparathyroidism has been employed to describe similar skeletal disturbances in the absence of the other features, including the altered calcium and phosphorus relationships. A case of dyschondroplasia and ectopic ossification, lymphoid hyperplasia, splenomegaly, gout, and rheumatoid spondylitis is presented. The authors propose to explain this syndrome on the basis of a developmental anomaly occurring at the time of parathyroid differentiation (approximately the eighth week of fetal life), when the cartilaginous anlagen of the osseous system is being elaborated. The mechanism whereby unfavorable influence is exerted upon parathyroid development, resulting in altered osseous structure in the absence of characteristic calcium-phosphorus changes, is not clarified.

PARSONS, Montrose, N. Y.

INTRACRANIAL HAEMATOMA CONCEALED BY LEAKAGE OF CEREBROSPINAL FLUID. CAMPBELL CONNOLLY, Brit. M. J. 2:1154 (Nov. 17) 1956.

Connolly points out that persistent rhinorrhea or otorrhea resulting from head injuries may greatly alter the classical clinical picture of acute intracranial hematoma. Such leakage tends to lower intracranial tension, so that intracranial blood clots may be easily formed. The intracranial tension may remain within normal limits, and the brain, although displaced, may not be compressed, so that there may be no deterioration of consciousness and no abnormal neurologic signs to suggest the presence of a hematoma. When the leakage of cerebrospinal fluid diminishes, special observation is important to detect hematomas, which, if present, may require immediate evacuation. Four illustrative cases are presented.

ECHOLS, New Orleans.

HYPERTENSIVE STROKES. A. W. D. LEISHMAN, Lancet 1:437 (March 2) 1957.

Leishman reports his studies on the clinical background of cerebral vascular accidents in a group of 234 hypertensive patients. In his series, 97 patients died as a consequence of hypertension; and stroke, which accounted for the deaths of 41, was the commonest cause. The study is concerned only with strokes which occurred before the age of 60 and is based on a survey of 31 cases in which the stroke was fatal and 25 cases in which the patient survived. No necropsies were done. Cerebral hemorrhage is liable to occur in any case in which the diastolic pressure is excessively high (150 mm. Hg or higher), but is also likely when blood pressure rather lower than this is accompanied by signs of severe renal damage. Cerebral hemorrhage, which occasionally develops as a late sequel to cerebral infarction, appears to be uninfluenced by either the severity or the character of the hypertensive condition and cannot therefore be foreseen. The study failed to reveal any special features by which a patient destined to develop cerebral thrombosis may be identified in advance. Cerebral hemorrhage due to hypertension is not easily explained in terms of atherosclerosis, and the clinical character of the cases studied suggests that fibrinoid necrosis is likely to be mainly responsible for cerebral hemorrhage before the age of 60. Since fibrinoid necrosis is potentially a reversible condition and almost certainly preventable, timely and effective hypotensive treatment should substantially reduce its incidence.

YASKIN, Camden, N. J.

SUBACUTE PROGRESSIVE ENCEPHALITIS: CLINICAL AND ELECTROENCEPHALOGRAPHIC OBSERVATIONS IN TWENTY-THREE CASES. A. M. HAMOLN, H. HERNGREN, W. S. VAN LEEUWEN, and O. MAGNUS, Rev. neurol. 94:8 (Feb.) 1956.

Of 23 patients with subacute sclerosing encephalitis observed, 15 died, 6 were severely deteriorated, and 2 have only recently developed their illness. The characteristic syndrome consisted of impairment of learning ability, periodic spasms or loss of muscle tone, language difficulty, and, finally, mental and physical deterioration and death. More than half the cases

began between 6 and 8 years of age. Death occurred in 3 to 27 months after the onset. The jerkings were of myoclonic variety, with flexor spasms of short duration, resembling electric chorea. The spinal fluid was a slight pleocytosis; the protein was increased to 60-100 mg. per 100 cc., and there was a "paretic" colloidal gold curve. The EEG revealed focal or bilateral delta activity. Pathologic examinations of seven cases revealed a variable degree of demyelination, gliosis, and mesenchymatous reaction affecting both the cortex and the white matter. In only three cases were there typical inclusion bodies.

BERLIN, New York.

Peripheral and Cranial Nerves

CHRONIC POSTHERPETIC NEURALGIA. L. S. VAN BLARICOM and G. HORRAX, J. A. M. A. 161: 511 (June 9) 1956.

The course of postherpetic neuralgia was studied in 35 patients, some of whom had suffered severely for more than three years. All of the patients were over 40 years of age. The sexes were almost equally affected. The thoracic nerves were involved most frequently and the trigeminal nerves next.

The authors believe that medical attention should be focused on the preventive aspect of postherpetic neuralgia, by perfecting the measures to reduce the severity of the acute attack (for example, therapy with chlortetracycline, chloramphenicol, and posterior pituitary injection U. S. P.) and to provide adequate relief of pain during this acute stage. It should be stressed that many of the procedures that fail significantly to relieve postherpetic pain are quite effective in treating the discomfort of acute herpes zoster.

Once postherpetic neuralgia has become established, the vicious pain cycle can be broken and the process prevented from spreading and acquiring momentum. The simpler procedures are often more effective than the major ones, and analgesic blocking is the most effective nonsurgical method. The earlier treatment is started, the greater the chances of obtaining relief.

Certain surgical procedures have been found to be effective in ameliorating this condition, and the experience of these workers has led them to select one with low morbidity as the initial step, proceeding to the next only if a failure is encountered.

ALPERS, Philadelphia.

FACIAL NERVE PARALYSIS AFTER GENERAL ANESTHESIA. J. E. FULLER and D. V. THOMAS, J. A. M. A. 162:645 (Oct. 13) 1956.

Fuller and Thomas report two cases showing partial facial paralysis after general anesthesia. In view of the fact that pharyngeal-respiratory obstruction is a very common occurrence during anesthesia and that pressure behind the mandible is frequently employed to relieve it, it is surprising that the facial nerve is not damaged more frequently.

The minor degree of weakness exhibited by the second case discussed suggests that it is not unlikely that minor paralysis goes unnoticed by both the patient and his doctors. Furthermore, there is considerable variation in the branching and the course of the nerve, and this may explain why it is rarely injured in this way.

While both the patients recovered in a relatively short time (in three months and three weeks, respectively), return of function might have been considerably delayed had retromandibular pressure been maintained for several hours. The authors emphasize the need for early tracheal intubation in patients whose airways can be maintained only by strong pressure applied to the lower jaw.

ALPERS, Philadelphia.

DIPHTHERITIC POLYNEURITIS—A PATHOLOGIC STUDY. C. M. FISHER and R. D. ADAMS, J. Neuropath. & Exper. Neurol. 15:243 (July) 1956.

Miller and Adams report the nervous system to be grossly normal and the central nervous system microscopically normal, as well, in six cases of diphtheria. Alterations were noted only in the peripheral nervous system, the characteristic finding being degeneration of the myelin of the nerve fibers within the posterior root ganglia (and the nodose ganglion of the vagus) and those portions of the nerve roots, both anterior and posterior, immediately adjacent thereto, that is, within about 2 mm. The myelin was replaced by fatty macrophages. An increase in cellularity was noted, and histiocytes and fatty macrophages predominated. The myelin degeneration was strikingly focal. The axis cylinders were essentially spared.

Evidence of an inflammatory reaction was almost entirely lacking. The large neurons in the ganglia and their capsule cells were normal. Anterior horn cells corresponding to levels of demyelination in the anterior roots showed no "axonal reaction."

SIEKERT, Rochester, Minn.

PATHOLOGY OF THE PERIPHERAL NERVOUS SYSTEM IN AFRICAN TRYPANOSOMIASIS. P. JANSSEN, L. VAN BOGAERT, and W. HAYMAKER, J. Neuropath. & Exper. Neurol. 15:269 (July) 1956.

Janssen, van Bogaert, and Haymaker present observations on the pathologic changes in trypanosomiasis. In all seven cases a meningoencephalitis was present. The site of predilection of the peripheral nerve involvement was the region of the dorsal root ganglion. Increase in cells, some of an inflammatory nature, was noted. Degeneration of ganglion cells and hyperplasia of capsular cells were seen in some instances. There were both Wallerian degeneration and focal demyelination (of Gombault-Stransky). Interstitial neuritis was common.

SIEKERT, Rochester, Minn.

Treatment, Neurosurgery

NEUROMUSCULAR BLOCKADE AND ARTIFICIAL RESPIRATION IN SEVERE TETANUS. L. V. FOYE JR., A.M.A. Arch. Int. Med. 99:298 (Feb.) 1957.

The successful treatment of a 20-year-old patient who developed tetanus seven days after a wound is presented. Initial therapy with antitoxin and antibiotics, supplemented with meprobamate and chlorpromazine, proved ineffectual in halting the increasingly violent respiratory spasms. Subsequently, a tracheotomy was performed, and relief of respiratory spasms by the combined use of depot curare and succinylcholine was achieved. A tank respirator was employed to compensate for the induced respiratory paralysis. Appropriate sedation, especially rectal tribromoethanol, was found to reduce the requirement for muscle relaxants. The authors point out that the combined use of muscle relaxants and artificial respiration has transformed the problem of management of tetanus into one similar to that of bulbar poliomyelitis, with the advantage that in tetanus the degree of respiratory paralysis is under iatrogenic control.

PARSONS, Montrose, N. Y.

GREAT AURICULAR NEUROTOMY FOR TIC DOULOUREUX. JOHN PENMAN and L. S. WALSH, Brit. M. J. 1:22-25 (Jan. 5) 1957.

Penman and Walsh conducted a study in which they subjected great auricular neurotomy to a controlled clinical trial, as recommended by Hill, in an effort to evaluate the procedure in the treatment of tic douloureux. Between August, 1954, and May, 1955, great auricular neurotomy was performed on 23 patients with severe tic douloureux, and during the same period 16 other patients with severe tic douloureux, comparable in all essentials with the disease in the first group, had no treatment. All 39 patients were scheduled for trigeminal injection, which they were told they could postpone if the pain abated sufficiently. All but 1 of the 23 (95.7%) treated by neurotomy requested trigeminal injection within 85 days, and all but 2 of the 16 controls (87.5%) had injection within 148 days. It was concluded that great auricular neurotomy has no effect on tic douloureux.

ECHOLS, New Orleans.

TREATMENT OF POST-HERPETIC NEURALGIA. W. R. RUSSELL, M. L. E. ESPIR, and F. S. MORGANSTERN, Lancet 1:242 (Feb.) 1957.

Russell and his co-workers report their experiences in 100 cases of postherpetic neuralgia. They conclude that postherpetic neuralgia can usually be relieved by concentrated treatment to reduce pain thresholds in the tissues adjacent to the scarred area. The removal of hyperesthetic zones is important, and for this the repeated use of procaine nerve block, and of a mechanical vibrator, is especially valuable. They found that it is quite easy to remove the hyperesthesia temporarily by blocking nerves or infiltrating the skin with procaine, and it is important to study without delay the effect of this procedure on the spontaneous pain. In many instances this simple procedure gives remarkable relief for several hours, and frequent repetition of the procaine block often leads to increasing periods of freedom, until relief may be permanent and the affected area no longer hyperesthetic. Procaine block of the nerves

supplying the skin adjacent to the scarred area may be specifically important. Thus, in ophthalmic herpes, block of the occipital nerves on the side involved, as well as of the supratrochlear and the supraorbital nerves on the opposite side, may be beneficial. Hyperesthesia can be abolished also by a mechanical vibrator. A vibrator with a vulcanite applicator, held lightly on a hyperesthetic area for 5 to 10 minutes, acts as a local anesthetic, without the trauma of a needle, and removes cutaneous hyperesthesia. It does the same with a tender scar.

YASKIN, Camden, N. J.

ACUTE POLYNEURITIS TREATED WITH CORTISONE. G. S. GRAVESON, Lancet 1:340 (Feb. 16) 1957.

Graveson reports eight cases of acute polyneuritis in seven patients treated with cortisone. In only one case was the disease not promptly arrested, and in this case the amounts of cortisone given were probably inadequate. The author states that cortisone is the remedy of choice in acute toxic polyneuritis, but must be given as soon as possible and in adequate doses. If treatment is started before paralysis becomes severe, the chances of rapid improvement should be good. Beyond this stage, it should stop the disease from progressing, but the over-all recovery time of the completely paralyzed muscles may not be shortened. For the average case the dosage suggested is 300 mg. daily for 2 days, 200 mg. daily for 2 days, and then 100 mg. daily for 10 days. If, after withdrawal at this stage, deterioration occurs, further treatment for another week or more may be needed.

YASKIN, Camden, N. J.

Encephalography, Ventriculography, and Roentgenography

EXAMINATION OF THE ATLANTOAXIAL JOINT FOLLOWING INJURY. G. JACOBSON and D. C. ADLER, Am. J. Roentgenol. 76:1081 (Dec.) 1956.

The anatomic characteristics of the atlantoaxial joint are such that its primary function is rotation, rather than the flexion and extension which are found in other joints of the spine. Injury to the atlas and axis frequently results in fractures and dislocations which are different in character from those encountered elsewhere in the spine. Jacobson and Adler present a method of examining the atlantoaxial joint segment of the cervical spine by roentgenograms and describe an entity which they call rotational subluxation of the atlantoaxial joint.

The atlantoaxial joint may be examined by means of (1) conventional roentgenograms made with the patient in the anteroposterior position with the mouth open and in the lateral position; (2) laminagrams, particularly those made in the anteroposterior position, and (3) motion, or functional, studies. The motion studies of the joint are made in the anteroposterior projection with films taken when the head is rotated to the right and to the left. The open-mouth view may be used, but often laminagrams are necessary to visualize the atlantoaxial joint spaces properly when the head is rotated.

Various lateral displacements of the atlas on the axis are described. They are evaluated by the appearance of the atlantoaxial joint in the anteroposterior open-mouth projection. Four different displacements have been named: (1) unilateral medial offset, (2) unilateral lateral offset, (3) bilateral offset, and (4) bilateral spread. Rotation of the normal atlantoaxial joint is described, and the roentgenographic findings during rotation are illustrated. Medial offset occurs normally on both sides during rotation.

Four cases are described in which there was a history of injury, in which medial offset of one side of the atlas was demonstrated, and in which no fracture or other evidence of injury could be found. All of the patients had symptoms of injury to the neck. In two cases the symptoms subsided spontaneously and the roentgenographic appearance of the joint returned to normal at the same time. In the other two cases the roentgenographic appearance of the joint remained abnormal and the symptoms persisted throughout the entire period of study. Jacobson and Adler believe that these four cases all illustrate a little-known syndrome which is best termed rotational subluxation of the atlantoaxial joint. Apparently, the symptoms in the neck persist until the subluxation is corrected or corrects itself. The roentgenographic findings in rotational subluxation are (1) medial displacement of one articular mass of the atlas with respect to the corresponding mass of the axis (unilateral medial offset) and (2) abnormal rotatory motion of the atlantoaxial joint.

WEILAND, Grove City, Pa.

VISUALIZATION OF THE BASILAR, CEREBRAL, AND VERTEBRAL ARTERIES DURING CAROTID CEREBRAL ANGIOGRAPHY. B. S. EPSTEIN and J. A. EPSTEIN, Radiology 67:738 (Nov.) 1956.

The basilar and cerebellar arteries are seldom visualized during carotid angiography. Epstein and Epstein report three cases in which such filling did occur. In the first case an occlusion of the internal carotid artery was present at its junction with the external carotid artery. No filling of the internal carotid artery occurred. The basilar and the superior and middle cerebellar arteries were visualized within the skull. The vertebral artery could be faintly identified in the neck. It was thought that the contrast medium reached the basilar and cerebellar arteries by reflex through the common carotid artery, the innominate artery, and the vertebral artery.

The second patient was an old woman who had injured her head when falling. She developed signs of an expanding lesion within the skull. A right cerebral angiogram visualized the basilar artery, the posterior cerebral arteries, the superior cerebellar arteries, and the left vertebral artery, in addition to the right cerebral vessels. The patient had a large left cerebral extradural hematoma and a small right subdural hematoma. She died after operation. Autopsy showed no abnormalities of the circle of Willis or the basilar artery. There was no thrombosis of the carotid arteries. It was thought that in this case the opaque medium reached the posterior circulation through the posterior communicating artery.

The third patient had a meningioma involving the right lesser and greater wings of the sphenoid bone. During the arterial phase of a right percutaneous cerebral angiogram the posterior communicating, posterior cerebral, basilar, and superior cerebellar arteries were filled.

WEILAND, Grove City, Pa.

RADIATION THERAPY OF NEUROBLASTOMA. W. B. SEAMAN and M. D. EAGLETON, Radiology 68:1 (Jan.) 1957.

All the early reports in the medical literature concerning neuroblastoma emphasized the rapid course of the disease and the uniformly fatal termination. Recent reports have intimated that the prognosis may be a little better than formerly thought. Surgical treatment of neuroblastoma is rarely feasible, because distant metastases or an unresectable primary tumor usually renders operation ineffective. Radiation therapy must be relied upon as the main therapeutic agent. Neuroblastoma is a particularly radiosensitive tumor.

Clinical examination of the patient and roentgenograms may be extremely valuable in helping to establish the diagnosis of neuroblastoma. However, a definite diagnosis can be made only by histologic examination of the tissue. It is sometimes difficult to determine the diagnosis even by this method. When the tumor is highly undifferentiated, it may be misdiagnosed as a lymphosarcoma. Seaman and Eagleton believe that all known foci of the disease should be treated by radiation therapy in any patient. Their treatment is aggressive, but the leukocyte count must be watched, and treatment must be discontinued if a marked leukopenia develops.

Seaman and Eagleton treated a series of 19 patients with neuroblastoma between 1949 and 1955. Of the 19 patients, 5 survived three years or longer after treatment. Two of the five surviving patients had histologically verified metastases at the time of treatment. The authors believe that a higher survival rate occurs in the younger age group of children.

WEILAND, Grove City, Pa.

News and Comment

GENERAL NEWS

Second International Congress of Neuropathology, Proceedings.—At the request of the Organizing Committee of the Second International Congress of Neuropathology, held in London, 1955, all reports, communications, and discussions presented to this Congress have been published by the Excerpta Medica Foundation under the title Proceedings of the Second International Congress of Neuropathology, London, 1955

These Proceedings consist of three parts: Parts I and II, containing 650 pages of text; Part III, containing 156 plates, giving all illustrations to the text.

This publication has been edited by Dr. W. H. McMenemey.

The Proceedings may be ordered from the Excerpta Medica Foundation, 111 Kalverstraat, Amsterdam, Netherlands, at the price of about £4 10s., fl. 50, or $12.50.

Books

BOOK REVIEWS

Selected Papers of Sir Gordon Holmes. By F. M. R. Walshe, Editor. Price, 20 s. Macmillan & Co., Ltd., 10 St. Martin's St., W. C. 2, London, 1956.

These ten papers, republished in homage to Sir Gordon Holmes on the occasion of his eightieth birthday, deal with three subjects with which his life and work have been particularly identified—the cerebellum, the cortical representation of vision, and visual orientation and attention. The papers concerning the cerebellum include the early paper on its connections with the inferior olives, that describing the form of cerebellar degeneration now known as the Holmes' type, the study of the symptomatology of cerebellar tumors, and the classic Croonian lectures of 1922 on the clinical symptoms of cerebellar disease and their interpretation, ending with the discussion of the functions of the cerebellum taken from the Hughlings Jackson lecture of 1939.

Many of these papers have not been readily available, and, if for no other reason, the guarantors of *Brain* have provided a real service in making them again obtainable by students of neurology; but this collection provides much more by bringing again forcefully to the reader the sagacity of a great neurologist. For here one can see the results of careful and persistent observations when coupled with a penetrating analysis, and here, also, one sees that the physician's ambit does not lie in the study of disease alone but that the study of disease leads to the appreciation of normal function, as is admirably demonstrated in the analysis of the function of the cerebellum as derived from the study of its diseases, and the working out of the cortical representation of vision from the study of cerebral injuries. Lastly, these papers may be commended to a new generation of medical writers because of the clarity of their prose and the logic of their plan, each conclusion being based upon adequate study and leading forward to the solution of yet another problem.

It is unfortunate that this collection had to be limited to only ten papers. Among the most unfortunate omissions are the Goulstonian lectures of 1915 on the spinal injuries of warfare, the papers on the disorders of sensation produced by cortical lesions, and the Victor Horsley Memorial lecture on the cerebral integration of ocular movements. It is to be hoped that the response to this collection may make it merely the prelude to the publication of the collected works of Sir Gordon Holmes.

CHARLES WELLS, M.D.

Physiological Foundations of Neurology & Psychiatry. By Ernst Gellhorn, M.D., Ph.D. Price, $8.50. Pp. 556. University of Minnesota Press, 10 Nicholson Hall, Minneapolis 14, 1953.

Gellhorn states in his introduction that the basis for this book consisted of the work that he and his colleagues have done. If this reviewer had not seen this statement, he would have missed a point which seems to explain much about this book: the interesting subdivision into topics, the emphasis in some areas as compared with others, and the total absence of some entries which this reviewer happened to have sought. The extensive correlations and the integrated discussion of very many investigations (which are strong characteristics of this book) could easily have led to a lack of recognition of the main motivation for its creation, since the coverage of the literature extends well into the sister discipline of neurophysiology. Particularly impressive are the sections on biophysical methodology and the insights gained therefrom. The same holds true for the entries on the motor cortex, on consciousness, on the autonomic functions, and on homeostatic mechanisms of the nervous system, which are all outstanding indeed.

The topics which this reviewer happened to seek, and did not find, are the ones related to hallucinogenesis and ataraxia, although it should be quickly conceded that the title of the book does not obligate the author to undertake excursions into these fields. Similarly, in view of the erudite discussion of adrenaline, acetylcholine, and acetylcholinesterase, one somehow expected a certain amount of comment on serotonin and amine oxidase.

The absence of such entries does not constitute a real drawback, in view of the excellence of the material which was chosen for inclusion: This book is exceedingly well written by a man who is greatly experienced in both teaching and investigation. It makes instructive and pleasant reading. The editorial work has obviously been painstaking, as is evident from all the details of this volume. The index is complete, and cross references are ample. The student as well as the teacher of modern neurophysiology cannot afford to be without this book. The investigator whom the writer probably had foremost in his mind will find, of course, many helpful ideas and techniques.

GEORGE C. COTZIAS, M.D.

Clinical Examinations in Neurology. By Members of the Staff of the Mayo Clinic. Price, $7.50. Pp. 370. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia, 1956.

Sixteen members of the Mayo Clinic neurology staff have contributed to this volume covering the clinical examination of the nervous system, both generally and in detail. This volume follows the usual pattern of outlining techniques in the taking of a neurological history and the examination of various cranial nerve functions, reflexes, strength, coordination of movement, and sensory perception. Included also are sections covering mentation, language and aphasia, autonomic function, electroencephalography, electromylography, and cerebrospinal fluid examination.

The descriptions of the various clinical testing procedures are covered in sufficient detail to be complete but not to the extent that they will overwhelm the medical student and house officer.

Included with this book is a series of charts for recording the examination which are used at the Mayo Clinic. These charts offer good suggestions for collecting and outlining data and should be of help to the reader.

FLETCHER MCDOWELL, M. D.

Modern Therapy in Neurology. By Francis M. Forster, M.D., Editor. Price, $12.00. Pp. 792. The C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1957.

"Modern Therapy in Neurology" discusses in detail the specific therapies of neurology, but perhaps more important by far is the strong emphasis placed on the plans for general management of the various neurological disorders. The amalgamation of the concepts of the "next step" in neurological therapy has been difficult, and this volume does much to give it impetus.

The cooperation of twenty-two authors has been enlisted by the editor to discuss under broad headings the therapy of infections, trauma, vascular disease, etc. Care has been taken to cover the therapy of all phases of the various disease processes and the complications which accompany them.

The sections covering cerebrovascular disease, seizure disorders, demyelinating disease, and basal ganglia are of special interest not only because they are the commonest disorders in neurology but because of the well-outlined program of management presented. These programs include not only the important pharmacological agents for therapy but suggestions for managing the patient's psychological problems, his family problems, and his working problems—phases of management which may be of much more importance to the patient than any others.

Important and controversial problems of therapy, such as anticoagulation in cerebrovascular disease, rest and vasodilatation in demyelinating disease, and the social aspects of the seizure disorder, are thoughtfully discussed.

This volume is somewhat longer than it needs to be and could be shortened by reducing the details covering the clinical aspects of the various disease states. However, in its present state the volume does present a needed addition to the reference books on neurology.

FLETCHER MCDOWELL, M.D.

Pain and Pleasure: A Study of Bodily Feelings. By Thomas S. Szasz. Price, $5.50. Pp. 255. Basic Books, Inc., 59 Fourth Ave., New York 3, 1957.

The nature of explanation often is different for one man than it is for another, particularly in the opening phases of inquiry. In this book a psychoanalyst presents his reflections on pain and pleasure; in keeping with the psychoanalytic tradition, the explanations he seeks maintain a sharp boundary between those things that are "bodily" and those that are in the realm of the "ego-experience" of the individual. The ability to deal with the rich world of

individual subjective experience is hard won and, understandably, often accompanied by dissatisfaction with the seemingly remote and sterile abstractions of those who seek monistic explanations in broad biological terms. The author frequently expresses this dissatisfaction—indeed, his rejection of the explanations of those who have sought to approach pain monistically and experimentally is a major theme of the book. From experimental studies two aspects of pain have been found to be measurable and, to a degree, predictable: the intensity of pain sensations, and bodily reactions to noxious stimulation and pain. For the author these two aspects omit the key element of explanation. Therefore, he dismisses much experimental work as irrelevant, when it may be only incomplete. The book presents no new experimental data, and the author limits himself to the complex but bounded microcosm of individual ego experience, thus from the monistic point of view failing to take us very far in bringing order into the intricate phenomena of pain, despite the ambitious chapter headings.

There is pressing need for attack on this problem from all levels, and the author is to be applauded for his efforts to deal with the subjective aspects of the pain experience. However, his rejection of differing points of view is too hasty, and he indulges in the vice of seeing neurotic dynamics in those who hold contrasting views. With these limitations in mind, the book is recommended as an addition to the small number of works concerned with these important subjects.

LORING F. CHAPMAN, Ph.D.

Benign Schizophrenia

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I wish to present a concept of benign schizophrenia as a dynamic mechanism of psychological defense. Bleuler[6] said (1922): "The term schizoid designates a type of mental nature and reaction which is more or less present in everybody, and in its morbid exaggeration constitutes schizophrenia." Schizophrenia, even in advanced cases, is a changing process that can move in either direction. Few cases show complete involvement of the ego; most have facets of the ego that are adequate despite the presence of schizophrenic defects.

Recent data on drug psychosis with lysergic acid diethylamide (LSD-25) (Hoch,[14] 1956) are significant. Upon receiving this drug, normal persons develop psychotic syndromes indistiguishable from schizophrenia: this suggests that a propensity for schizophrenia is present in everyone. Administered to persons with mild or moderate schizophrenia, LSD-25 aggravates the psychosis. Moreover, the concurrence of organic psychosis and some qualities of schizophrenia is well known in alcoholic hallucinosis, dementia paralytica, and arteriosclerotic, senile, and toxic psychoses. Thus, schizophrenic disorganization may arise from undermined organic supports. Conversely, schizophrenia may be allayed by organic means, such as electroconvulsive therapy, lobotomy, lobectomy, and tranquilizing drugs. At the other pole, we have experimental schizophrenic-like psychoses induced by isolation from sensory stimuli (Lilly,[17] 1956), as well as psychoanalytic data about schizophrenia as a process. From these observations, we should not conclude that schizophrenia is either (*a*) organic in etiology, and due to a cerebral lesion or chemical toxin, or (*b*) wholly psychogenic, and that biological factors are inconsequential. Rather, we should recognize that psychological balance is a product of total personality organization, and defects in either the psyche or the soma or both may be significant for faulty functioning of the ego.

Definition

Schizophrenia is a psychotic reaction and must be defined in the framework of a general concept of psychosis. Part of the difficulty lies in the unwarranted aim to fit one label to all aspects of complex human personality and the failure to recognize that many permutations and combinations of psychosis, psychoneurosis, and character patterns may coexist. Another confusing element about psychoses is that the loss is rarely complete, so that intact parts function alongside the defects and, in turn, the intact portions of the ego make restitutive efforts to fill the gaps. Consequently, secondary symptoms, such as delusions, confabulations,

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and affective disturbances, come to the fore and may be mistaken as the prime disturbances.

Organic psychosis, the classical prototype of psychosis due to neurological damage, is characterized by losses of intellectual and emotional capacity. A cerebral defect syndrome, it is a mental disorder with regressed degrees of irrational, illogical, or immature behavior. It shows faulty perception or judgment of reality, or an inner lack due to a loss of control, understanding, or executive ability. It reflects a loss of advanced behavior patterns, with a return to earlier ones. In these terms, organic psychosis is not a completely new state but a partial or total regression to a former one. For example, in senile psychosis, it is said that the person becomes childish again. The basic feature of organic psychosis is regression from late to earlier patterns of behavior. Organic psychosis is essentially psychological deterioration due to disorganization of the neurological foundations of the ego.

Therefore, the infantile psyche may be considered the baseline for psychoses. In a sense, the newborn infant and child are originally like organic psychotics; however, they develop out of this state in the natural course of growth. Of course, the normal infant is not to be considered psychotic; only its same immature features, if seen out of place in later life, form the characteristics of psychosis. Similarly, congenital organic mental deficiency is probably the only true congenital psychosis, since development is arrested from birth.

Psychogenic psychosis arises from psychological disturbance in factors that originally contribute to psychic maturation or maintain psychic stability. A basic identity of functional and organic psychoses lies in the breakdown of fundamental psychological organization. Both are marked by regression to earlier ways of thinking. In place of neurological damage, the root of psychogenetic disturbances is anxiety, which either retards development in early life or disorganizes established development in later periods.

The present concept of functional psychosis is about half a century old, developed by Kraepelin, Bleuler, and Freud contemporaneously. Kraepelin [16] (1899) described two functional psychoses: manic-depressive psychosis and dementia precox. Bleuler [5] (1911), seeing the essence of dementia precox as a fragmentation of previously built-up personality, changed the name to schizophrenia. The shattering of the acquired fabric of thinking was the distinctive feature; the other symptoms, such as autistic fantasies, catatonia, and delusions, were secondary elaborations. As early as 1894, Freud attributed psychosis to defects in the ego. He subsequently recognized the resurrection of primitive processes and spelled out the dynamics of regression to primary narcissism, primary process thinking, and the projective mechanisms of delusional thinking (Freud,[10] 1911).

A new concept, in addition to the breakdown of established ego structure after adolescence, is that schizophrenic processes may involve undeveloped ego, with a type of arrest, retardation, or confusion. These include the childhood autistic syndromes of Kanner [15] (1944), infantile anaclitic depressions of Spitz [20] (1946), symbiotic psychoses of Mahler [18] (1952), development lags of Bender [1] (1955), and others. Furthermore, insights about the detailed structure of schizophrenia have been gained from psychological projective tests. These elicit small indicators of schizophrenic processes, such as minor degrees of autistic, paranoid, and narcissistic thinking, that are seldom suspected clinically.

Schizophrenia may be defined as a functional psychotic reaction characterized by varying degrees of psychological immaturity, and arising from confusion or arrest of psychological development, or breakdown of established organization of the psyche to cope with reality. The basic feature is a disorder of thinking. However, this may be obscured by secondary emo-

tional and restitutive symptoms, such as affect disturbances or delusions, derived from intact parts of the ego. The base line of psychosis is the original undeveloped psyche of the infant, and the prime characteristics of schizophrenia, whether involving a fragment or a major part of the ego, are infantile primary process thinking and narcissistic preobject relations to reality.

Phenomena of Benign Schizophrenia

My concept of benign schizophrenia is that it is a transitory or isolated process and serves a defensive function in supporting the ego, even in so-called normal persons, to prevent the greater disorganization of malignant schizophrenia. It is benign in the same sense that we speak of benign and malignant tumors and, as such, may be relatively insignificant or serious, depending upon their tempo of activity or location. Some benign schizophrenic features may flare up momentarily in reaction to an immediate situation, and recede promptly. Others are isolated features, surrounded and often hidden by healthy traits. Variations in degree of benign schizophrenic reactions can be found along a scale from few minimal ones to moderate, or even maximum quantities just short of malignant schizophrenia.

Benign schizophrenic manifestations are discernible in many everyday reactions of children and adults and in character traits, in character (psychopathic) disorders, in psychosomatic conditions, in impulsive and behavior disorders in childhood, in the course of psychoanalytic treatment, and in psychological tests. I offer only a few general illustrations here (clinical case material will be presented elsewhere).

The outstanding example of transitory benign schizophrenic features is the dream. Dreams show regressed ego mechanisms of frank psychosis (Freud,[12] 1938). While dreaming, we are all schizophrenic and use primitive mechanisms of wishful thinking. Basically, sleep is a narcissistic regression which involves separation from reality. Daydreams and fantasies are also unrealistic and have a wishful emotional quality.

Normal doubts and suspicions of unfriendliness, and even mild ideas of reference, have qualities of persecutory delusions. Food phobias in children are often based on fantastic ideas of being poisoned. What adult has not felt at some time on entering a strange group that he might not be wanted or would not be liked? Defensive hostile ideas and irritable moody reactions may follow. Of course, there may occasionally be some reality in the situation, but more frequently it is mostly projection. Catatonic-like episodes of negativism and defiance are common in the child, such are breath holding, head banging, sulking, refusal to talk, and stubbornness. Outbursts of temper and tantrums are momentary lapses of sanity; crimes of passion are recognized by the law as temporary insanity, and the words "mad" and "angry" are synonymous colloquially.

Related to grandiose delusions are dreams of glory, secret ideas of grandeur. Both children and adults under pressure use excuses and rationalizations to confabulate or deny reality in self-deluding fashion to cover difficulties. Lapses of memory and prolonged amnesia are direct denials of reality. An extreme example is "blacking out" or psychogenic fainting at a great emotional shock. Ecstasy and elation may temporarily go far beyond reality. That young lovers are not sane is a commonplace; they overvalue their partners, and reality after the honeymoon is often sobering.

The other type of benign schizophrenia is schizophrenic character traits; these are more persistent and fixed. Though of schizophrenic coloration, the benign quality rests in being isolated and circumscribed. The process is generally stationary and confined to a limited field without invading other parts of the personality. Unlike symptoms and typical of character traits, these do not disturb the individual and are accepted as legitimate features of the ego. Such traits are found to a degree in all people and hide

under the label of immaturity. Some are a handicap; others have positive value.

So-called ambulatory schizophrenias (Zilboorg,[22] 1941), borderline and schizoid characters (Brill,[7] 1928), contain isolated schizophrenic traits alongside adequate ego features. Criminals, perverts, eccentrics, paranoids, apathetic persons, and shy, seclusive people are psychotic in their typical features. The pervert, for example, has immaturely regressed or has not developed further than pregenital infantile sexuality. At root, the pervert has no insight and uses this pattern as a defense against his anxiety. The symptom of perversion is a direct psychotic-like expression of infantility and has many qualities of a delusion. The same applies to the antisocial features of criminals, eccentrics, and paranoids—isolated patterns of schizophrenically disorganized ego.

On the positive side, many successful people owe their achievements to schizophrenic character traits. Determination in the face of great hardship is frequently rooted in psychotic attitudes regarding money, fame, or love. Many acts of heroism would not be possible with a full awareness of reality. The personalities of genius (e. g., Beethoven, Lincoln, van Gogh) often include psychotic facets; these traits do not detract from their creations, and some argue that these traits have partially made the contributions possible. The caricature of the absent-minded professor as crazy with his distracting preoccupations is not far from the truth.

Psychoanalytic practice provides unique opportunities to observe transient benign schizophrenic processes in *status nascendi* reacting directly to increased anxiety. Although a distinct differentiation of psychoneuroses and psychoses was claimed in the past, wider application of analysis has changed these ideas; more and more we see our cases as mixed. Under stress conditions of analysis, psychotic defenses often appear temporarily. Many of these processes arise as new or increased resistances, especially to the transference. Such is the psychotic quality of direct acting-out denial found in prolonged obstinate silences, missing appointments, fleeing from analysis, and attempts at suicide. Some analysands project paranoid hostility in reaction to an interpretation but have sufficient insight to recognize their unreasonableness. Feelings of depersonalization, unrealness, and blankness are not infrequent. Such are the psychotic regressions in analysis that Winnicott[21] (1955) describes and Grinker[13] (1955) warns against. Frequently, psychoneurotic symptoms cover psychotic patterns, and caution must be employed in our uncovering techniques. Similar functions of defense against psychotic reactions are found in psychosomatic conditions. In a sense, one must have care in analysis to treat first the psychosis and then the psychoneurosis; every analyst probably copes with a degree of benign psychosis in each case.

Function of the Benign Schizophrenic Reaction

The primary task of the organism is survival, and its main index of difficulty is pain or anxiety. Psychiatric conditions stem from states of anxiety and represent psychological maneuvers to bear or overcome it. The major generic psychiatric conditions may be classified as adjusted personality (health), character (personality) disorder, anxiety (affect) neurosis, psychoneurosis, and psychosis. Adjusted personality is the total ego make-up and capacity to handle life situations relatively adequately. It represents the "health" of the individual (Blau,[3] 1954). At best, healthy personality is only more or less adequate, never perfect.

When a situation threatens the organism, anxiety appears and calls forth defense reactions. Until the problem is resolved, a physiological and psychological anxiety state exists. If the personality is inadequate or the threatening situation is too great, the anxiety is prolonged or exaggerated, and a

chronic anxiety (affect) neurosis develops (Blau [2,3]; 1952, 1955).

An anxiety situation may be solved in a real or fantastic fashion. Normally the danger is overcome or avoided by a change in the outside situation or an inner readjustment. But when a real solution is impossible, the only course is retreat into fantasy, which basically involves the mechanism of denial of reality. Either a partial compromise with reality or a full denial requires regression which permits the individual to solve his problems in a nonrealistic childish (psychoneurotic) or infantile (psychotic) manner.

Thus, regression is a retreat from the front line of reality when defeat is imminent. However, all regression is not the same but varies in quality, degree, and duration. The amount of regression necessary depends upon the relative extent of danger to the particular ego and its capacities. The retreat is to a former secure position (libidinal fixation point); and if one step is not enough, further retreat is needed. The regression may be to minimal, moderate, or major psychoneurotic defenses or, if more is required, to minimal, moderate, or major psychotic defenses. One can thus outline a gradient of regressive defenses, a scale from mild psychoneurotic to severe psychotic.

The psychotic defense, the complete denial of reality, is the most regressive. It has the most primitive form, dates to early pregenital infantile patterns, and is a stage below the psychoneurotic oedipal defense of partial childish denial of reality. It indicates that the organism requires a larger degree of ego disorganization to evade painful reality. The malignant psychoses are extreme morbid breakdowns of established ego structure with progressive disintegration. Although it is a psychological distortion, the schizophrenic defense is nevertheless the lesser evil because it ensures basic survival. Like psychoneurosis, it is a natural dynamic defense against anxiety.

Comment

The purpose of diagnosis is not merely to label a syndrome. The name should at best have meaning with regard to etiology, treatment, and prognosis. Diagnosis is equivalent to the step of generalization in the scientific formula of observation, classification, and generalization. Therefore, if benign phenomena have valid common denominators with the malignant, the similarity must be recognized for better understanding.

The term schizophrenia describes the nature of the process adequately; it designates a serious disruption of the psychic thought organization. However, a view of benign levels changes it from a static nihilistic to a dynamic hopeful one. To recognize positive defensive aspects of the reaction, both in its benign and malignant forms and in its identity with immaturity, enlarges our vista. We need not avoid the term because of its past connotations. A new name for benign forms would tend to confusion.

A fuller concept of schizophrenia will not dilute it, only add a more comprehensive view of its genesis and meaning. The relevant issue is whether there is a significant relationship among these varied phenomena and whether the basic process is truly schizophrenic. The importance of the diagnosis does not rest in its presence, because schizophrenic mechanisms are more or less omnipresent. Most significant is its quantity or quality—whether acute or chronic, circumscribed or diffuse, stationary or progressive, whether part of the basic character or merely symptomatic, spontaneously recoverable or requiring treatment.

The recognition of schizophrenic processes in many psychiatric conditions, for example, throws new light upon the therapeutic immobility of behavior disorders, criminality, perversions, and character disturbances. The trend has been to invoke organic and hereditary explanations. But if the typical psychopathology is recognized as schizophrenic in a limited area, better under-

standing emerges. Remarkable in these cases is the combination of well-oriented logical behavior parallel with abnormal bizarre traits. But what are the latter if not fragments of schizophrenia?

Furthermore, schizophrenia seems to be the only functional psychosis, very like de Sauvages' concept of vesania [19] (1763). More and more psychiatrists find that manic-depressive psychosis is not a separate group but schizophrenia with outstanding emotional symptoms. The better prognostic attitude is not lost in this view; rather, a more optimistic attitude is developing for the whole of schizophrenia.

The mixture of psychoneuroses with schizophrenia poses special problems. We are indecisive and remiss in diagnoses like severe neurosis, mixed neurosis, pseudoneurotic psychosis, and latent and borderline psychosis. Psychoneurotic reactions can coexist with the psychotic; the former may even screen the latter. But each should be recognized for what it is. The psychoneurotic process is an entirely different functional reaction in that a partial link with reality is maintained. The psychoneurotic regression is to the more mature, oedipal period of ego development; it includes a degree of object relationship, and the conflict is internalized. In psychoneurosis, the conflict is between ego and id, while in psychosis it is between ego and reality (Freud,[11] 1924). In another context, Freud[9] (1905) recognized this contrast, indicating that "neuroses are, so to say, the negative of perversions." The perversion, a direct acting out of instinctual id impulses, is essentially a psychotic manifestation, a correlation which Freud seems to suggest in a footnote in the fourth (1920) edition. Fenichel[8] (1945) states:

> Neuroses represent a regression to infantile sexuality; the psychoanalysis of neuroses brought about the understanding of infantile sexuality. Schizophrenia represents a regression to the primitive levels of the ego; psychoanalysis of schizophrenia will permit understanding of the evolution of the ego.

Increasingly, success in psychotherapy of schizophrenia has been reported. However, as distinctly separate processes, the psychoneurotic and psychotic require entirely different approaches in technique, which have to be clearly formulated theoretically and tested in practice.

Summary

The thesis is presented that benign schizophrenia, like the psychoneurotic mechanism, is a universal ego defense process against anxiety found varyingly from infancy throughout life. It occurs as transitory episodes and isolated character traits short of a malignant process. Its basic nature is immaturity of thinking due to arrest, regression, or breakdown of ego structure, with a distortion of the individual's relation to reality. Schizophrenia is considered the only functional psychotic process. This dynamic view of schizophrenia as a defense serves to detoxify the concept of functional psychoses and offers significant implications for normal development, classification, and treatment.

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Depressive Affect and Endocrine Functions

Blood Levels of Adrenal Cortex and Thyroid Hormones in Patients Suffering from Depressive Reactions

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The significance of the adrenal cortex and the thyroid gland in the adaptation of the body to stressful life situations has been a subject of increasing interest in recent years. Evidence for the importance of these functions for vital adaptation has been reviewed previously[1] and in more recent publications.[2,3] We have reported that hospitalized psychiatric patients had elevated levels of plasma hydrocortisone (17-hydroxycorticosterone; 17-OH) and protein-bound iodine (PBI). The hydrocortisone levels were significantly higher than in controls; the PBI levels were elevated, but not significantly, when compared with those for normal control subjects. When the cases were evaluated from the viewpoint of either the intensity of emotional distress or the extent of personality disintegration, there seemed to be a correspondence between the height of the level of each hormone and the degree of clinical disturbance of the patient. Exceptionally high hormone levels were associated with very intense distress accompanied by depressive affect, retarded behavior, and evidence of extensive personality disintegration.

From these leads we undertook a fresh study designed to examine more closely a population of patients with depressive reactions. We were interested in learning whether a significantly large group of depressed patients have elevated hormone levels, how long they remain elevated, what psychological processes are closely associated with elevated hormone levels, if any, and whether these levels decrease with decreasing emotional disturbance.

Subjects

Thirty-three patients were studied after admission to the psychiatric section of a general hospital. Subjects were selected for this study (1) if the attending psychiatrist had made a diagnosis of depressive reaction, and (2) if the house officer (psychiatric resident) independently made the same diagnosis. No patient was excluded from the study because his depressive reaction was too severe or too mild. Several patients were excluded because of recent electroconvulsive therapy elsewhere.

As a group, the patients paid for their own hospitalization, had either high school or college education, and lived in middle-class communities of Chicago. The ages ranged from 26 to 67, with an average age of 49 years. Seven of the thirty-three subjects were men. Twelve of the patients were admitted to the most disturbed units of the hospital initially, while the majority were admitted directly to units of less disturbance: nineteen to the least disturbed closed unit and two to an open unit.

Most of the patients were in good physical condition, but two had diabetes mellitus; one had simple achlorhydria; one had benign prostatic hypertrophy; one had syphilis, and one had old fractures of the vertebrae. One of the patients

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who had controlled diabetes mellitus also had mild arteriosclerotic heart disease.

Method

Patients were seen for initial interviews early in hospitalization, i. e., within the first 96 hours. Each patient who remained in the hospital was seen for two subsequent interviews, at weekly intervals. Blood samples for hydrocortisone and PBI were drawn at 9:00 a. m. and 12 noon, bracketing each psychiatric interview. These interviews, which lasted from 40 minutes to 1 hour, were designed to provide an assessment of the patient's current emotional state, his predominant feeling experiences in terms of distress and depression. Descriptions of the behavior, facial expressions, and motor activity were used by the psychiatrists as confirmation of the verbal communications of the patients and of judgments about psychomotor activity. The interview was designed to be neither stressful nor therapeutic, but at times explanations and reassurances were required. In general, the interviewer encouraged free expression of feeling but did not attempt to probe for unconscious material. Questions of a specific nature were asked toward the end of the interview.

Special note was made of (1) the difficulty patients had in adjusting to the hospital setting; (2) discomfort over the feeling of loss of status in family and community from being hospitalized; (3) fear of unfavorable disposition, such as legal commitment to a mental hospital, and (4) disintegrating psychological defenses, as indicated by the feelings of unexpected loss of reality. The first 10 patients interviewed indicated by their statements that these four areas of adjustment were very important to them during the early phase of hospitalization; therefore, these items were specifically looked for in interviews with all subsequent patients.

From the clinical data, two psychiatrists made independent ratings for distress, depression, retardation, and agitation on a scale of 0 to 5, where 0 represented the absence of the state and 5 represented the most extreme example in the physicians hospital experience. Consensus or average ratings were the basis for all final scores.[4] For some phenomena no quantitative rating was feasible but only a check of "present" or "absent." This presence-or-absence type of rating was used for (1) difficulty in adjustment, (2) loss of status, (3) fear of disposition, (4) disintegrating defenses, (5) inability to cry, and (6) tearfulness.

Biochemical results were kept completely separate from the psychiatric observations until all of the ratings had been completed. Determinations of PBI were made in duplicate from a 12 cc. clotted-blood sample by the Grossmann-Grossmann method,[5-7] and the hydroxycortisone determinations were made from a 23 cc. heparinized sample by Nelson and Samuel's method.[8,9]

Results

Hormonal Levels of the Entire Group of Depressed Patients Compared with Those for Normal Subjects.—When the entire group of depressed patients is compared with normal subjects, there is a difference in the mean hydrocortisone levels, demonstrating that depressed patients have higher levels. The mean hydrocortisone level of depressed patients is 19.5γ per 100 cc., or 59% higher than the controls ($P = <0.0001$). The nine patients judged to have the greatest degree of depressive affect have a mean hydrocortisone level of 23.7γ per 100 cc., a value approximately 92% higher than that for the normal controls.

PBI levels show no such distinctive difference, the mean being 5.7γ per 100 cc. for depressed patients on the first occasion and 4.9γ for the normal controls. Although the mean PBI level of the patients is higher than that of the controls, the relationship is not statistically significant. The nine most depressed patients have a mean level of 6.7γ per 100 cc., 36% higher than that for normal controls (Table 1).

Initial Day of Testing.—Analysis of Subgroups: Analysis of subgroups characterized by high degrees of intensity of emotional distress, psychomotor retardation, or personality disintegration reveals that there is correspondence betwen the height of the level of the hormone and the clinical disturbance of the patient. For example, when the patients are rated according to the degree of emotional distress, it is found that the mean hydrocortisone level for the 8 most distressed patients is 24.5γ per 100 cc. and the mean for the 10 least distressed patients is 17.7γ per 100 cc. ($P = <0.05$; one-tailed). On the other hand, for protein-bound iodine, the mean for the most distrssed group is 6.0γ per 100 cc., and that

TABLE 1.—*Plasma Adrenocortical Hormone and Blood Thyroid Levels of Depressed Patients and Controls*

Group	Plasma Hydrocortisone					Serum PBI				
	N	Mean, γ/100 Cc.	Standard Deviation	*t*	*P*	N	Mean, γ/100 Cc.	Standard Deviation	*t*	*P*
Control subjects	24	12.3	6.1	4.05	<0.0001	9	4.9	1.5	1.39	N.S.
All depressed patients	33	19.5	7.0			33	5.7	1.7		
Most depressed patients	9	23.7	..			9	6.7	..	..	..

for the least distressed group, 5.4γ per 100 cc. (*P* N. S.).

The seven patients rated highest for psychomotor retardation have a mean hydrocortisone level of 25.3γ per 100 cc. When this is compared with those patients having no retardation (mean=18.3γ per 100 cc.), the significance is similar ($P<0.05$). The mean PBI level for the 7 most retarded patients is 7.2γ per 100 cc., compared with 5.1γ per 100 cc. for 10 depressed patients who have no retardation ($P<0.05$).

Six patients complained of an inability to cry during the initial interview. Their mean hydrocortisone level is 23.8γ per 100 cc. Eleven of the patients cried frequently during the initial interview. Their mean hydrocortisone level is 18.2γ per 100 cc. The correlation between those unable to cry and those who cried is <0.05. The mean PBI values show no relationship.

The presence of disintegration of defenses was clearly seen in five patients. When this group is compared with the 13 patients who had no disintegration of defenses, the hydrocortisone values are 23.0γ and 16.9γ, respectively. There was not a large enough number to test probability (Table 2).

Psychological Subgroups of Depressed Patients: Perhaps the most outstanding result of the clinical ratings is the separation of depressed patients into distinct subgroups: (1) those who are deeply depressed, retarded, and unable to cry; (2) those who are moderately depressed, mildly retarded or overtly agitated, and tearful, and (3) those who are mildly depressed but are not in general experiencing psychomotor discharge, crying, or inhibition of these two expressions. Considering all clinical data for the first occasion, it is seen that when the ratings for "distress" and "depression" are compared there is a high degree of correlation. "Retardation," when present, is also statistically correlated with high "distress and depression."

A continuum involving all of the clinical cases is useful in defining these groups of depressed patients. At one end of the continuum is the group of patients having

TABLE 2.—*Statistical Analysis (t-Tests) of Adrenocortical Hormone Levels for Various Subgroups of Depressed Patients*

Groups	Plasma Hydrocortisone					Serum PBI				
	N	Mean, γ/100 Cc.	Standard Deviation	*t*	*P*	N	Mean, γ/100 Cc.	Standard Deviation	*t*	*P*
High distress	8	24.5	8.75	1.80	0.05 *	8	6.00	1.11	0.87	N.S.
Low distress	10	17.7	7.43			10	5.30	1.59		
High retardation	7	25.3	7.99	1.90	0.05 *	7	7.24	2.05	2.35	0.025 *
No retardation	10	18.3	7.10			10	5.05	1.56		
Inability to cry	6	23.8	7.51	1.81	0.05 *	6	5.98	1.42	0.89	N.S.
Crying	11	18.2	5.16			11	5.38	1.14		
Disintegration	5	22.9	8.80	1.52	—	5	5.62	1.12	0.06	—
No disintegration	13	16.9	6.12			13	5.67	1.66		

* One-tailed tests.

TABLE 3.—*A Continuum of Depressed Patients and Their Mean Hydrocortisone (17-OH) and Protein-Bound (PBI) Values*

Depression and Retardation	Unable to Cry	Crying	Neither	Total		Unable to Cry		Crying		Neither	
						9 A. M.	12 N	9 A. M.	12 N	9 A. M.	12 N
High	6	1	1	8	17-OH	27.0	21.9	(20.6)*	(17.4)	(13.6)	(12.0)
					PBI	6.3	5.9	(5.6)	(7.1)	(4.6)	(4.8)
Mod.	1	8	5	14	17-OH	(17.8)	(30.9)	18.7	13.3	18.0	13.7
					PBI	(3.9)	(4.0)	5.4	5.7	7.0	6.5
Low	0	2	8	10	17-OH	--	--	15.1	13.7	18.3	14.0
					PBI	--	--	5.1	5.1	5.5	5.3
	7	11	14	32							

$\chi^2=22.72$; $P<0.001$.

* Parentheses contain values of one patient and are not means.

the characteristics listed in (1) above. Next are those patients having the characteristics in (2), and completing the continuum is the patient group described in (3). The hydrocortisone levels reflect the distribution of the clinical ratings. In the case of PBI, the highest levels are not the uppermost left values but the values for those patients who are moderately distressed and retarded and who complain neither of being unable to cry nor of crying frequently. Table 3 is one method of demonstrating this relationship.

Subgroups: Attitudes and Defenses: Some patients were frightened of hospitalization, expressing fear or anger toward the hospital, the staff, and other patients; many patients were concerned about what their families, friends, and business or social associates would think, and many feared that their eventual disposition would be permanent institutionalization. Some maintained their psychological defenses, but others presented overt signs of personality disintegration. As the course in the hospital continued, patients were able to learn from one another that the usual length of hospitalization was one to two months, that treatment was effective in most cases, and that an adjustment to the strange environment could be made. Several patients found relief from their first visit with relatives; some, when they felt they had been able to help another patient; some, when they found a particular activity which would occupy their time, and others, after they had established a positive attitude toward their physician, a member of the hospital staff, or the Institute. With a few exceptions, there was an amelioration of attitudes and a strengthening of defenses by the beginning of the second week of hospitalization.

The ratings of "attitude toward the hospital" correlate with the degree of "distress" with which the patients were suffering at the time; that is, in general those who had negative attitudes about the hospital were suffering more intensely ($P<0.05$). This holds true for "status" to a slighter extent ($P<0.10$). The ratings for "disintegrating defenses" are correlated with "distress" to a striking degree ($P<0.001$), and the degree of anxiety about disposition is also correlated with distress ($P<0.05$), as was expected. There is no correlation of "attitude" and "status" with "retardation," for apparently those who were most retarded were not concerned with the hospital.

Statistical Treatment of Initial Occasion: Because of the number of correlations present in this study, it was felt that the data should be treated in a more complete manner. A correlation matrix of all variables is introduced for this purpose. Table 4 is composed of "Pearson r correlations" for all the subgroups in the initial occasion. One may observe (1) the high positive correlations between the 9:00 a. m. and the 12:00 noon chemical values for both hydrocortisone and PBI; (2) the relationship of depression, distress, retardation, inability to cry, and disintegration to hydrocortisone

TABLE 4.—*Correlation Matrix: Psychiatric and Chemical Variables of Patients with Depressive Reactions*

	Distress	Retardation	Inhibition of Crying	Disintegration	Agitation	Crying	Neg. Attitude	Loss of Status	Anxiety over Disposition	Hydrocort., 9 A. M.	Hydrocort., 12 N	PBI, 9 A. M.	PBI, 12 N
Depression	0.927‡	0.778‡	0.654‡	0.668‡	0.502‡	−0.025	0.244	0.196	0.301*	0.279	0.382†	0.329*	0.320*
Distress		0.767‡	0.642‡	0.731‡	0.434‡	0.061	0.371†	0.328*	0.408†	0.261	0.349†	0.168	0.195
Psychomotor retardation			0.706‡	0.694†	0.273	−0.213	−0.008	−0.099	0.135	0.465‡	0.428†	0.326*	0.243
Inhibition of crying				0.465‡	0.252	−0.384†	0.194	0.213	0.212	0.336†	0.530‡	0.036	−0.023
Disintegration					0.465‡	0.075	0.441‡	0.477‡	0.352†	0.303*	0.356†	−0.032	−0.047
Psychomotor agitation						0.124	0.391†	−0.089	0.409†	0.259	0.272	−0.129	−0.103
Crying							0.079	0.046	0.228	−0.311	−0.306	−0.188	−0.034
Expression of neg. attitude								0.774‡	0.314*	0.142	0.247	−0.352*	−0.360†
Expression of loss of status									0.317†	−0.077	0.174	−0.349†	−0.277
Anxiety over disposition										−0.101	0.005	−0.393*	−0.241
Plasma hydrocortisone 9:00 A. M.											0.456‡	0.011	−0.080
12 N												−0.223	−0.329*
PBI 9:00 A. M.													0.927‡

* <0.10 <0.05.
† <0.05 <0.01.
‡ <0.01 <0.001.
§ <0.001.

subgroups; (3) the poor relationship of crying, agitation, negative attitude, loss of status, and anxiety over disposition to hydrocortisone subgroups, yet a negative relationship to PBI, which is at times statistically significant.

A multiple correlation is completed for hydrocortisone and PBI. The weights to be used in the prediction of PBI are depression (1.016), retardation (−0.211), attitude (−0.302), status (−0.181), disposition (−0.380). Hydrocortisone is subjected to the same treatment, and it is found that either psychomotor retardation or inability to cry gives as accurate a prediction as the combination of any of the other variables.

Changes During the Initial Morning: The mean level for hydrocortisone at 9:00 a. m. is 19.5γ per 100 cc., falling to 15.8γ per 100 cc. by 12:00 noon on the first occasion. The PBI values on the first occasion remain essentially the same: 5.7γ per 100 cc. for both the 9:00 a. m., and the 12:00 noon mean levels. The standard deviation for the 9:00 a. m. hydrocortisone level is 7.01. Several of the patient's levels change more than twice this standard deviation.

In this connection, an interesting nutritional finding presents itself. Those patients who gave histories of low nutritional intake, and who were observed to be poorly nourished on admission to the hospital, almost invariably have a decrease of hydrocortisone levels from the 9:00 a. m. to the 12:00 noon sample, while those patients who gave a history of no nutritional problems, and who were considered on admission to be in good physical health, almost invariably have an increase in level of hydrocortisone or the level remains approximately the same. A *t*-test between the group of patients with "poor nutrition" and the group of patients with "good nutrition" is 2.98, with a probability of <0.01. These groups represent the average run of patients rather than the most disturbed versus the least disturbed. The high and low values of hydrocortisone in these groups with defined nutritional states are reversed[10] (Table 5).

TABLE 5.—*Plasma Adrenocortical Hormone Levels: Change from 9:00 A. M. to 12 Noon*

	N	17-OH Level 9:00 A. M. Mean	17-OH Leve 12 Noon Mean	Dif.	*t*	*P*
Patients with no nutritional problem	7	15.5	19.5	—4.0	2.98	0.01
Patients with nutritional problem	10	20.8	15.1	5.7		

Second Period of Testing.—The psychiatric interview and the blood studies were repeated one week later. By this time, however, noticeable changes had taken place in the patient group. Nine patients had been discharged; some patients had been transferred to less disturbed units, and the psychiatric ratings had decreased from 30% to 42% for most variables. The two exceptions were "crying," which decreased 6%, and "anxiety over disposition," which increased. More specifically, "distress" decreased 42%; "depression," 33%; "retardation," 35%, and "disintegration," 34%.

Hormone levels decreased for both the 9:00 a. m. and the 12:00 noon mean levels. The hydrocortisone has dropped to 17.7γ per 100 cc. at 9:00 a. m. and 12.1γ per 100 cc. at 12:00 noon. The PBI mean levels have decreased to 5.4γ per 100 cc. at 9:00 a. m. and 5.2γ per 100 cc. at 12:00 noon.

The patients seen on the second occasion may be divided into two groups: those who received electroconvulsive therapy (EST) during the first week of therapy and those who received other types of therapy. There were 10 who received no EST. Their mean hydrocortisone values are 16.4γ per 100 cc. at 9:00 a. m. and 10.5γ per 100 cc. at 12:00 noon. The PBI values have also fallen: The non-EST group level at 9:00 a. m. is 5.3γ per 100 cc., and at 12:00 noon it is 5.4γ per 100 cc. The 13 patients who received EST had a mean hydrocortisone level of 18.8γ per 100 cc. at 9:00 a. m. and 13.2γ per 100 cc. at 12:00 noon. The PBI group level at 9:00 a. m. is 5.5γ per 100 cc., at 12:00 noon 5.0γ per 100 cc.

The EST group may be characterized according to initial emotional ratings as having greater distress, depression, retardation, inability to cry, and disintegration than the non-EST group, the latter having higher values for agitation and crying. This difference exists throughout the second and third periods of testing.

Third Period of Testing.—At the time of the third period of testing, two weeks after the beginning of the experiment, the group had changed considerably. A total of 21 patients had been discharged or excluded. Of the remaining, the psychiatric ratings decreased further. The ratings for distress dropped 53%, depression 52%, retardation 67%. The associated crying had stopped, as had the complaints about status, and only

TABLE 6.—*Adrenocortical and Thyroid Hormone Means for Depressed Patients During Course in the Hospital*

		First Occasion			Second Occasion			Third Occasion		
		N	9 A. M.	12 Noon	N	9 A. M.	12 Noon	N	9 A. M.	12 Noon
All patients	17-OH	33	19.5	15.8	23	17.7	12.1			
	PBI	33	5.7	5.7	23	5.4	5.2			
No EST	17-OH	10	(20.2)*	(10.1)	10	16.4	10.5			
	PBI	10	(5.7)	(5.7)	10	5.3	5.4			
EST	17-OH	13	(18.5)	(16.8)	13	18.8	13.2			
	PBI	13	(6.7)	(6.4)	13	5.5	5.0			
No EST	17-OH	5	(18.6)*	(11.0)	4	(18.2)	(10.3)	5	17.8	10.9
	PBI	5	(6.4)	(6.4)	4	(5.5)	(5.6)	5	5.4	5.1
EST	17-OH	6	(17.1)	(12.5)	6	(15.9)	(12.5)	6	28.1	12.7
	PBI	7	(7.3)	(7.2)	5	(6.2)	(5.1)	7	6.4	6.4

* Figures in parentheses are means of those patients who were tested on subsequent occasions.

one patient continued to have a "negative attitude" toward the hospital.

The hormone levels of the patients in the non-EST group remained at approximately the level of the second occasion. However, when the EST group is separated out, it is seen not only that this is again the more emotionally disturbed group, but also that the mean hydrocortisone level for 9:00 a. m. has risen 8.6γ per 100 cc. from the mean on the first occasion (10.4γ per 100 cc. from the second occasion). The 12:00 noon mean for hydrocortisone remains at approximately the same level. The PBI mean levels for the EST group have also increased—more than 1γ per 100 cc. for both the 9:00 a. m. and the 12:00 noon mean values above the second occasion.

When the EST patients in the third occasion are traced to the first and second occasions, it is found not only that the patients form a special group in terms of the emotional ratings but also that their hormone levels respond in a particular manner. An extreme example is represented in Table 7 (cf. with lower half of Table 6). The high level of PBI initially declines during hospitalization, and the hydrocortisone values begin at moderately low levels, rise abruptly, and end at moderately high levels. This pattern is seen in all of the EST patients' hormone levels. The psychiatric ratings of the EST patients are above the mean throughout, but not so high as those for the most disturbed group on the first occasion of testing.

Pharmacological Effects.—It has been reported that the administration of barbiturates lowers the level of hydrocortisone.[11] Nine of these patients received barbiturates in moderate doses (0.1 to 0.2 gm.). One received 0.3 gm. during the night prior to testing. The mean hydrocortisone levels for 9:00 a. m. and 12:00 noon are 22.1γ and 16.6γ per 100 cc., respectively. These values are somewhat higher than the means for the entire group. Therefore the effect which was noted on our previous study is not seen in this instance.

A number of other drugs were used; however, there are not a sufficient number of patients receiving any single drug to make significant comparisons. The small groups of two, three, and four patients receiving chlorpromazine, meprobamate, or chloral hydrate do not appear to deviate from the mean values of the entire group. No patient received paraldehyde, and the PBI values of the one patient who received organic iodides prior to hospitalization were eliminated.

Comment

Initial Day: Meaning of Elevated Levels.—When all the chemical data of the initial day of testing are taken into consideration, depressed patients may be characterized as having elevated hydrocortisone levels. This elevation is statistically significant when compared with the value for the "normal" control subjects. The PBI levels are also elevated above the controls, but there is not a significant statistical difference. If the hydrocortisone levels are divided into three groups according to the rating for "depression," the highest mean hydrocortisone level accompanies the "most depressed patients" (Table 1), the lowest mean hydrocortisone level (not shown) accompanies the "least depressed patients," and the level between accompanies the "moderately depressed patients."

In examining the important elements of a depression, we see from the analysis of the subgroups that the most outstanding relation is between those patients who are

TABLE 7.—*Plasma Hydrocortisone (17-OH) and PBI Levels During All Occasions of Testing of One Patient Who Experienced Decreasing Emotional Disturbance*

	First Occasion		Second Occasion		Third Occasion	
	9 A. M.	12 Noon	9 A. M.	12 Noon	9 A. M.	12 Noon
17-OH	16.7	12.5	36.0	15.6	24.2	18.7
PBI	11.9	11.3	11.9	8.5	8.0	8.0

suffering intensely (deeply depressed, retarded, unable to cry, with disintegration of defenses) and the height of the level of hydrocortisone. Depressive affect in the presence of inhibition of psychomotor activity or inhibition of crying is accompanied by increased blood levels of hydrocortisone. In contrast to this, patients of less severe disturbance are those who are able to cry, are sometimes agitated, and verbally complain about their status and fears of the hospital or disposition. In this patient group the hydrocortisone is at a lower level. The division of patients into their distinct groups on the basis of the psychological material is presented in Table 3. The variables seen in Table 4 which indicate inhibition of expression are positively correlated among themselves and with the hormone variables. Those variables which indicate expression of affect have in no instance a significant positive correlation with the chemical variables. This contrast of relationships indicates that discharge of affect is important not only in the clinical status of the patient but also in the physiological response.[12,13]

Interpretation of Changes During the Course of Therapy.—Of those who remained in the hospital and received psychotherapy without EST, the hormone levels followed a gradually declining course through the periods of testing, reaching levels which were decidedly lower, but still above that of the controls.

The EST patients followed a strikingly different course. The hormone levels at first appear to decrease and then to increase. However, on examination of the seven subjects who were tested, on three occasions, it is seen that they are distributed between the "most disturbed" and the "moderately disturbed" groups, the initial levels of hydrocortisone are moderately low, and the PBI levels are high. As therapy progresses and psychiatric evaluation indicates improvement, the hydrocortisone increases to a high level and the PBI decreases to a more moderate level. These seven patients had suffered from prolonged stress in the form of depression, in contrast to those patients in the no-EST group. Rather than suggest that EST stimulates the adrenal cortex, via the hypothalamus and the pituitary,[14,15] we feel that the change was stimulated by an alteration in the psychological state of the patient.

Depression seems to be a matter of withdrawal associated with intense internal suffering. If this suffering is not expressed, the adrenal cortex responds with increased blood levels of hydrocortisone, the usefulness of which is unknown at this time. Heightened adrenal cortical activity may be looked upon as a second-order stress response; the thyroid activity, as a third-order stress response (adrenal medulla activity being an immediate, or first-order, stress response). If the stress lasts for some time, the hydrocortisone decreases and the PBI increases, suggesting a form of exhaustion of the adrenal cortex and an increase of thyroid activity. Therefore findings in depression should differentiate between acute and chronic. When the depression begins to lift, the hydrocortisone is elevated, the PBI declines, and this change is associated with a greater capacity for expression. Attention should be called to the fact that in the period of recovery, when the patient is able to express himself, the danger of suicide increases.

Methodologic Problems.—There was no apparent difference in the mean hydrocortisone and PBI levels of those patients who had organic disease and the means of those who did not. There was no difference between the levels for the premenopausal women and those for the postmenopausal women, and also no difference between the men and the women. Thus, we included all of our data in the statistical analysis.

The loss of patients from the follow-up studies was considered unavoidable. Most of this loss was accounted for by the recovery of the patient, so that he became inaccessible to us. It was not possible to have patients return to the hospital for follow-up interviews and chemistry studies.

The scattered use of drugs is an uncontrolled variable. Not only were drugs used intermittently, according to the needs of the patient, but they were often used in combinations largely determined by the unit practice.[16]

Summary

The mean hydrocortisone levels of depressed patients are elevated as compared with levels for normal controls. Protein-bound iodine levels are also elevated, but not significantly.

In general, the more emotional distress the patient is undergoing, the higher the hydrocortisone level. There is a significant relationship between those patients who are suffering intensely, are retarded, and unable to cry, and those who are less depressed, agitated, and crying. The hydrocortisone levels parallel this relationship, the most intensely depressed and retarded group having distinctly higher levels than the less depressed group.

A correlation matrix of the first occasion is presented to demonstrate existing relationships among subgroups of the study.

The multiple correlation indicates that (*a*) the variable of psychomotor retardation, or inhibition of crying, may be used for the prediction of elevated hydrocortisone levels, and (*b*) when protein-bound iodine levels are predicted, multiple factors should be used for weighting the prediction.

On the subsequent occasions of testing the ratings of depression, hydrocortisone and PBI levels fall. However, this was not true of the EST group, and an explanation is suggested for the relationship of function of the adrenal cortex and the thyroid in depression.

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Early Infantile Autism in Identical Twins

Report of a Case

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Early infantile autism, a form of schizophrenia first appearing in infancy, was described by Kanner in 1944.[1] In the hope that a study of this condition might shed clearer light on the etiology of schizophrenia, much interest has since then been shown in early infantile autism.[2-5] Two cases have been reported in which this condition occurred in identical twins,[6,7] and a third such instance is here reported. This illness characteristically appears in only one child of any family, and its occurrence in identical twins is hence of particular interest.

A striking withdrawal from interpersonal activity is the prime feature of early infantile autism. As early as the fourth month of life the child may show apathy to the attention of those caring for him. As he becomes older, this withdrawal from emotional contact with people becomes more obvious. The autistic child has a marked interest in things as opposed to persons. He ignores the people around him and concentrates his attention on inanimate objects. An intense preoccupation is shown in maintaining the sameness of things; he becomes upset if the order of the objects in his room is changed, and he will set about putting them back in their previous arrangement. He may sit for hours scarcely moving, or he may engage in stereotyped play.

Often such children show a remarkable interest in music and a precocious ability to learn melodies and songs. Repetitive, superficially meaningless physical movements are common. Memory is usually excellent, sometimes phenomenal.

Language is often very sparse, and one-third develop no speech at all.[8] Those who talk may have a peculiar confusion in learning to use "you" and "I" correctly. These children are often unresponsive to the speech of those around them and may, for a time, be considered deaf.

The prognosis is very guarded, and it is not clear whether treatment is effective in altering the course of the illness. The prognosis of those children who do not speak by the age of 5 years is extremely poor,[9] but is somewhat better in those who have learned to talk by this age. As these children grow older, they take on the appearance of childhood and adult schizophrenics in whom catatonic features predominate.

The etiology cannot be clearly stated. The parents of autistic children are described as emotionally cold, compulsive people, often with intellectual and professional accomplishments. Though it is assumed that early interpersonal trauma is important in producing this condition, it is often difficult to explain why such a quantitatively severe collapse of interpersonal relationships has occurred. One of our cases occurred in a family with 12 children, of whom the patient was a middle child, and the only one who had difficulty in making an adequate social adjustment.

Early infantile autism charcteristically occurs in only one child in a family.[6] It is of interest, therefore, that Sherwin and Bakwin have each reported it in identical twins. We have also observed it in a set

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of identical twins, who are described below. Extensive studies have been made on schizophrenia in adult twins, and much of the evidence for genetic and constitutional factors in adult schizophrenia is based on accumulated data on the relative incidence of schizophrenia in identical and fraternal twins. When one adult twin has schizophrenia, the illness will be found in the other twin in 86% of identical twins, but in only 15% of fraternal twins.[10] The figures for schizophrenia first diagnosed between the ages of 5 and 11 years show an incidence in identical twins of 71% and in fraternal twins of 17%.[11] Such data on early infantile autism, or on infantile schizophrenia in general, are not available.

Report of Case

Jean and Joan were identical twin girls, who were first seen in the psychiatric outpatient clinic of the Children's Mercy Hospital when they were 2 years 11 months old. Their parents had brought them to the clinic for evaluation of their unusual development and behavior.

The mother was delivered of these twin girls after a pregnancy of seven months and three weeks. The membranes had ruptured spontaneously, and labor lasted 40 hours and was not severe. The mother had no illnesses during the pregnancy. Both parents are 25 years old and in good health. There is no family history of mental illness. The father is a truck driver, and both parents stopped their education at the end of high school.

Jean weighed 4 lb. 4 oz. (1928 gm.), and Joan weighed 3 lb. 2½ oz. (1332 gm.), at birth. No postnatal cyanosis or jaundice occurred. For the first seven weeks of life these children remained in a hospital because of their prematurity.

Both children were somewhat slow in psychomotor development. Jean sat up at 8 months, stood at 16 months, and walked at 18 months. Joan sat up at 8 months, stood and walked with help at 1 year, and walked without help at nineteen months.

During the latter half of the first year of life the parents began to notice abnormalities in the behavior of both girls. They were listless, apathetic, and not as active physically as normal children. They did not respond to speech, and the parents wondered if they were deaf. Neither twin made an attempt to talk; Joan at one time is stated to have been able to say "mama," but other than this neither one has ever said a word. Their only articulations consisted of plaintive moans or feeble cries. The parents complained that the children were unattentive to everyone around them and never tried to imitate anyone. Both children spent a great deal of time sitting or standing motionless in corners.

As they grew older, their emotional isolation from all other persons became more obvious. Jean would sit for hours staring at her fingers. At other times she would place her fingers in a stair-step position and gaze at them for long periods of time unless someone came to move her hands. The children showed no interest in each other. They did not play with each other or with other children. If one of them accidentally infringed on the activity of the other, they became agitated and moaned and walked away. They played mechanically with simple toys, but never interacted with other persons in their play. Physical examination in the general pediatric clinic was unremarkable, except for an internal strabismus of the left eye in both children. Laboratory data were unremarkable. The children had identical coloring in their skin, hair, and eyes, and were indistinguishable from one another on inspection. No neurological abnormalities had been noted on examination in the neurology clinic. Because of their inability to communicate in any manner, psychometric and psychological testing could not be carried out. The attitude of the parents seemed to be one of earnest concern for their children; no obvious disturbances of attitude toward the children were found.

On psychiatric examination the autistic behavior of the children was striking. Neither one paid any attention to any other person in the room. Neither child spoke a word. They from time to time moaned or uttered plaintive cries in a low pitch. Each one wandered about the room at a slow pace, threading her way around people but paying no attention to them. Occasionally they would wave their hands to and fro in an aimless manner, with their arms abducted and the forearms flexed. Jean was observed in the stair-step clasping of the hands that her parents had described. No organized play was seen; they appeared interested in the physical characteristics of each toy but unable to use it for its intended purpose or to integrate it into play activities. Neither child responded to anything the examiner said and appeared oblivious to speech. It was clear, however, on careful observation, that they alertly perceived background noises, such as the sound of a closing door. No rapport of any nature could be established. They paid no attention to each other or to their parents, who were also in the examining room part of the time.

Comment

If interpersonal factors are important in causing early infantile autism, it would appear necessary that they be severely traumatic in nature and that they occur in the first several months of life. The emotional damage would have to be very marked to produce severe pathology with such profound, and often irreversible, consequences. Definite data on such damage are often unobtainable; one must usually rely on the parents as the sole informants, and they often describe no unusual events. The existence of early emotional trauma in individual cases is often hypothesized on the basis of what appear to be the personality characteristics of the parents when the child is seen several years later.

On the other hand, some observers consider that genetic and constitutional factors are also important in schizophrenic illnesses.[12] If this is so, and if it applies to early infantile autism, a significant body of data on this problem will be the accumulated case material dealing with its relative incidence in identical and fraternal twins. So far as I have been able to discover, early infantile autism has not yet been reported in fraternal twins, whereas it has now been described in three sets of identical twins.

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The Effects of Taraxein on a Patient in Analysis

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Introduction

Heath and co-workers have injected taraxein, a substance (protein fraction) obtained from the serum of schizophrenic patients, into nonpsychotic volunteers, inducing symptoms characteristic of schizophrenia. Most of the volunteers were prisoners in the Louisiana State Pententiary at Angola, La. This report will describe the effects of taraxein* on a resident in psychiatry who at the time he received the test material had been in psychoanalysis for one and a half years. He reported his reactions in the 175th session. This subject is a much better reporter of subjective feelings than any of the subjects heretofore used, and his verbalizations, because of the prolonged patient-doctor relationship, can be much more accurately evaluated.

Background

In a number of published articles and presentations now in press, Heath and co-workers have described their ideas concerning the etiology of schizophrenia.[1-4] They believe, as do Rado and his co-workers,[5] that it is a genetically determined disease and that the behavioral changes are due to underlying metabolic and physiologic alterations. Heath's group has presented preliminary data indicating that the defect is probably based on a faulty enzymatic system "responsible for impaired metabolism of normally occurring endogenous substances — apparently of the amines, i. e., adrenaline, norepinephrine, and others.[3]" They "feel that faulty metabolism of these chemical constituents results in the formation of accumulation of substances which act upon the brain as a type of toxin, producing the behavioral patterns characteristic of schizophrenia."[3]

They further believe that this inborn biological defect, together with psychogenic environmental factors, produces the varying clinical pictures of schizophrenia, and, while psychotherapy is sometimes of great value, that no treatment of schizophrenia can be completely successful without an attempt to remedy the underlying metabolic disorder.

While studying oxidizing enzymes,[6-8] Heath and co-workers isolated a qualitatively different substance, which they named taraxein, from the serum of schizophrenic patients. Injecting this substance into nonpsychotic volunteers,[9,10] they were able to induce symptoms characteristic of schizophrenia. This substance could not be obtained from the serum of nonpsychotic subjects.

Report of Case

The subject of this taraxein experiment is a psychiatric resident, age 27, who has been in psychoanalytic treatment for one and a half years. He entered analysis because of mild feelings of depression and of inadequacy. Another primary reason for psychoanalytic treatment was to obtain help in his work with patients. The only personality characteristics which are relevant to this report are his marked concern about making a good impression upon people in a variety of circumstances. His fear of humilation is directly relevant to his reactions under taraxein. Although he does wish to please people in authority, it never reaches the point of marked ingratiation or of self-humiliation in order to curry favor.

Subjective Report.—Following is a partial abstract of the 175th session, mostly in the patient's own words, on May 28, 1957, the day after he received taraxein. There is the inevitable distortion produced in making notes, but it is a reasonably close approximation of the patient's words.

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* This batch of taraxein was processed by independent chemists not connected with Tulane University.

"As you know, I volunteered for the experiment. (Why did you?) I was curious (pause) . . . I got scared; I don't know why. They had two test doses. One was not potent with the monkeys; the other was. They gave the less potent test dose to an intern. He had a slight reaction, nothing convincing. I was to get the potent test dose, one which had made a monkey catatonic for several hours. They gave me an injection, I thought it was normal saline†. I was trying to control my anxiety and to control myself, not to be suggestible. I was talking real fast, as I usually do when I'm anxious. When I got the injection, I remember my veins stood out. My heart started to beat fast. My head felt as if it were swollen. My head and face felt flushed. It lasted a couple of minutes maybe.‡ About three minutes later I started feeling different. My thought processes slowed down. I couldn't think clearly. Was it normal saline? I asked myself. I wondered whether they were trying to trick me into a hysterical reaction. I was curious. I wanted Charlie (here he is referring to Dr. Charles Feigley, the doctor who administered the injection) to know I had a reaction; yet I wanted to cover up, to keep talking, so he would not notice I was having trouble thinking. Yet, I wanted him to know that I was reacting. I tried to find out whether he was aware of my reaction by asking him leading questions.

"Then I realized that I had forgotten completely where my arms were. I had them outstretched in a flexed position, and I had left them there for some minutes. That was my first indication that I wasn't functioning well. I told myself, 'Be careful.' I became real guarded. Sometimes I couldn't think of anything to say, and I couldn't carry on a conversation. Sometimes, because I was afraid of saying anything, I tried to talk on a superficial basis. I had a very funny feeling in my face. I couldn't feel my face exactly or my lips. I kept feeling for my lips as if they weren't there.

"After it was all over and we were going to lunch (this was 45 minutes later), I felt real distant from everybody. I was sitting there, not like one of the group, but like an observer. I didn't participate at all. I started coming out of it about an hour and 20 minutes after the injection. (Here I interjected some questions to try to get amplification of the preceding material.) Yes, I could carry on a conversation, but only with great difficulty. I would leave things in the middle. Thoughts would pass by as if my brain was not working right. When I was having it, I thought it was a hysterical reaction and kept saying to myself, 'I have to control myself.' (Did anything feel strange, anything other than you have mentioned?) No, but I wasn't worried about anything. Before we started I was conscious about other people on the other side of the mirror. (Here he was referring to the one-way mirror.) But after the injection, I was only aware of Charlie and myself. (What were your feelings toward Charlie?) M. said I looked tense; Charlie said I was flat, that I was scrutinizing him all the time. I remember watching him but didn't feel angry toward him. I developed a headache toward the end. (Can you tell me more about the blocking of your thoughts?) Well, one usually has more than one thought in one's mind at a time. Your thoughts are usually faster than your words. It was the opposite here; I had to wait for my thoughts to catch up. I could function; yet I felt real detached from everything. (What about the content of your thoughts?) I was worried about what Charlie was thinking—that I was having a reaction I shouldn't have. I expected to get the saline first. (Are there any other reasons why you think you volunteered?) I was curious. I wanted to see myself whether the stuff worked. (Do you think it was possible that you wanted to please the research group?) Just the opposite. I didn't want to react to what I thought was normal saline. What would people think of me if I had this reaction to normal saline?"

Objective Report.—Following are the observations of Dr. Charles Feigley, who administered the taraxein.

"In recounting the events occurring when F. took the taraxein, I thought I'd mention what happened as I saw it from the time of the actual decision.

"The first part of the discussion about details of the injection took place with F. present; this was almost immediately recognized and he left with me, chatted for about 10 minutes before actually getting started. During this time he appeared a little embarrassed but otherwise chatted amiably and seemed to be taking the situation quite well.

"During the preliminaries and the photographed interview and up to the injection I was unable to see any sort of change in him. We chatted about several things, one of them being a trip C. had proposed to him—Europe in the fall, I think.

"Blood was taken from one arm, which he then flexed; I then gave the taraxein to him in the other arm. He leaned back slightly, with both arms flexed, and we kept on talking; right away I felt he must be uncomfortable with both arms

† The double-blind technique was employed, as usual. There were always two syringes, one with test material, the other with a control substance. The subject knew this.

‡ Probably a reaction to the ammonium sulfate in the solution.

flexed so tightly and leaned over and straightened both arms, without any resistance or waxiness on his part.

"Throughout the rest of the interview I had a feeling something was wrong with him, tried to get him to tell me about what was happening to him, and felt dissatisfied about him throughout. He appeared quite conscious of me to the extent I felt slightly uncomfortable; he turned some of the questions around and asked them of me. He asked one question as to why I wanted to know the details of C.'s proposed trip, and he seemed belligerent as he did. He appeared self-conscious, to be trying to keep the conversation going, and I thought to myself that he was acting as if he had met me for the first time. During the silences he was uncomfortable, fidgety, and scrutinized me quite closely. On several occasions he glanced up quickly, looked at me searchingly, and made some comment about how closely I was watching him. Now this seemed unusual to me, for, although I was observing him, I was rather tired and hot, and felt, in fact, that I was observing him much less closely than before. He glanced furtively at the microphones and the opposite two-way mirror and picked up a little gadget that looked like a TV station changer, spent a few minutes explaining why he was toying with it, wondering what it was. At this point I thought he definitely was furtive, as if he was trying to tell me something, or as if there were some hidden meaning about the microphones and this gadget. During the silences, and while talking at times also, he seemed flat affectively, and I noticed his facial musculature sagging; from time to time he would sort of pull his facies together as if to present himself better, and this seemed to take considerable effort. His foot touched mine several times, and he seemed irritated that I should be in his way. Otherwise, I just felt frustrated that something was going on in him that I couldn't elicit.

"Afterward he seemed to want to be close to me and once asked me how he looked; I evaded the question. On the way to lunch I was aware of him for a time, then, although he was with us, walking close to me, I noticed that he was silent, still flat, and that I was considering him a nonentity. I felt as if I was ignoring him, because as a person he wasn't there. This appearing apart from the crowd continued throughout lunch. In the cafeteria line he was lethargic, did not comment about the food, as he usually did, picked only a salad and hamburger steak, and then at the table only toyed with them. He said he was tired, and during lunch stared out the window at the top of the opposite building. When asked, he said that he felt far away, as if he was looking back at himself. He did seem detached, far away, and maintained the flat affect. This same behavior continued on the way back to school, and he remarked several times how tired he was, how he'd like to go home to sleep; I thought these statements were perseverations."

Comment

The subject's reactions consisted mainly of (1) blocking of thought processes, (2) autism (a feeling of being apart from the group and of difficulty in participating), (3) bodily estrangement, as seen in his lack of awareness of the positions of his arms in space and his uncertainty about the presence of his face and lips, and (4) suspiciousness, namely, his fear that he was being tricked. He was frightened by the idea that he was responding with schizophrenic symptoms to isotonic saline.

The first three sympstoms were found to a greater or less extent in all of the volunteers receiving taraxein. Suspiciousness occurred in a number of them. Some of these subjects also had very evident rage reactions. Several volunteers displayed clear-cut accessory symptoms, e. g., mutism, waxy flexibility, auditory hallucinations, bizarre delusions, etc. This subject, however, was a much better reporter than any of the previous subjects. In addition, since he was known by his analyst to be an honest person, given to self-scrutiny, his report was considered to be highly significant. This was particularly true because it fitted in so well with the objective observations of his behavior during the hour and 20 minutes following the injection. The validity of his reporting is also increased, I believe, by the fact that he was trying so hard not to have a reaction. In order to avoid ridicule, he was trying to normalize his reactions. Therefore, this reaction cannot be considered hysterical. The symptoms were not dramatic or self-dramatizing. In fact, they were quite the opposite, as it took close scrutiny to know that something unusual was occurring. It was the covert, subjective effects of the drug that were most noteworthy, hence the importance of a subject who is an experienced reporter of introspective data.

To be sure, this single experience in a single patient could not by itself be considered scientifically significant. Nonetheless, when it is coupled with the reactions of the previous volunteer subjects, it becomes highly significant, although it is clear that more experiments of this kind are necessary. It is particularly necessary to have these carried out by a number of different research groups.

Summary

A patient who has been in psychoanalysis for a year and a half volunteered to receive a test dose of taraxein. His reactions included blocking of thought processes, autism, and bodily estrangement, as well as flattening of affect, all of which fit Bleuler's description of the primary or fundamental symptoms.[11] This reaction was deemed worthy of reporting because the subject's inner feelings were verbalized with much greater clarity and precision than were the subjective reactions of the previous subjects. In my opinion, there is every reason to believe in the authenticity of the reported feelings.

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Studies in Pharmacologic Psychotherapy

III. Effective Psychotherapy During Drug-Induced States

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This paper is the third of a series dealing with the theory and technique of what we have called, for want of a happier terminology, pharmacologic psychotherapy.[1,2] By pharmacologic psychotherapy we mean the procedure of combining appropriate psychopharmacologic and psychologic strategies in the treatment of emotionally disturbed patients.

What we propose to describe in the present instance are the specific psychotherapeutic strategies which seem to be required if pharmacologic psychotherapy is to be at all successful in the treatment of relatively refractory patients who are suffering from severe psychoneuroses and personality disorders.

The Cases

The refractory patients on whom we shall base our observations are 31 in number. We have treated these patients with pharmacologic psychotherapy for varying intervals of time over the past eight years. All 31 we think of as refractory or relatively inaccessible to treatment on two counts: First, the psychopathology in each case was one which is generally accepted as resistant to treatment of any type, and, second, in every instance the common psychotherapies, including psychoanalysis, had been tried with no apparent success. That is, before his experience with pharmacologic psychotherapy, each of these patients had been previously exposed to either psychoanalysis or psychotherapy on at least two separate occasions. Yet insofar as we could judge, the common psychotherapies either had failed to bring any appreciable relief to these patients or had made their state more unbearable than it had been prior to treatment.

We present something of the history of our refractory group in Tables 1 and 2. Table 1 concerns 19 patients who came to us after undergoing psychoanalysis without any demonstrable improvement. Table 2 describes the 12 additional members of our total group, all of whom had previously failed to respond favorably, in this case to psychotherapy.

Failure of Previous Experience with the Common Psychotherapies

When the members of our group first consulted us, all were suffering from severe psychoneuroses or personality disorders of long standing. (Tables 1 and 2 list the specific diagnoses.) All 31 patients were markedly anxiety-ridden, multivalent, depressed, and nihilistic in attitude, with a high incidence of severe obsessional reactions. Each was in a state of acute neurotic misery. All 31 had rigid personality structures and severe disturbances of adaptation on every level of experience—occupational, social, and intrapsychic. Using the schema suggested by the American Psychiatric Association,[4] we estimated that 15 of our 31 patients had a 30% to 50% disability and that the remaining 16 members of the group were suffering from an over-all impairment of 50% or more (Tables 1 and 2). As time went on, we concluded, in agreement with Hoch that these patients, taken as a whole, were cases of "pseudoneurotic schizophrenia." * We were further struck by the

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* In a discussion of our work before the meeting of the American Psychopathological Association on June 2, 1956, Hoch called this series of patients typical cases of "pseudoneurotic schizophrenia."[3]

TABLE 1.—*Status of Nineteen Refractory Patients After Termination of Psychoanalysis*

Case No.	Disorders *	Degree of Impairment †	Verbal Communication ‡	Length of Psychoanalysis	School of Psychoanalysts §
1	Passive-aggressive personality	xxxx	++	7 mo.	Freudian, M.D.§
2	Passive-aggressive personality	xxxx	— — —	3 yr.	Freudian, M.D.§
3	Passive-aggressive personality	xxx	++	2 yr.	Freudian, Ph.D.
4	Passive-aggressive personality	xxx	— — —	6 mo.	Freudian, M.D.§
5	Passive-aggressive personality	xxx	+++	1½ yr.	Freudian, M.D.§
6	Passive-aggressive personality	xxxx	+++	6 mo.	Freudian, M.D.'S (2) psychiatrists (3)§
7	Passive-aggressive personality	xxxx	+++	2 yr.	Adlerian, M.D.§
8	Passive-aggressive personality	xxxx	— —	2 yr.	Adlerian, M.D.§
9	Passive-aggressive personality	xxx	— —	1 yr.	Adlerian, M.D.§
10	Passive-aggressive personality	xxx	— —	1 yr.	Adlerian, M.D.§
11	Passive-aggressive personality	xxx	–	7 mo.	Freudian, M.D.§
12	Passive-aggressive personality	xxxx	— —	2½ yr.	Freudian, M.D.§
13	Obsessive-compulsive reaction	xxx	+++	2½ yr.	Freudian, M.D., 2 yr.§ Jungian, M.D., 6 mo.
14	Obsessive-compulsive reaction	xxxx	— — —	2 yr.	Freudian, M.D.§
15	Obsessive-compulsive reaction	xxxx	+++	4 yr.	Freudian, M.D., 1 yr.§ Adlerian, M.D., 3 yr.§
16	Obsessive-compulsive reaction	xxx	— —	1 yr.	Freudian, M.D., 6 mo.§ Adlerian, M.D., 6 mo.§
17	Anxiety reaction	xxx	+++	3 yr.	Adlerian, M.D.§
18	Anxiety reaction	xxx	—	2 yr.	Freudian, M.D.§
19	Schizoid personality	xxxx	+++	3 yr.	Freudian, Ph.D.

* For nomenclature, see "Diagnostic and Statistical Manual; Mental Disorders," American Psychiatric Association, 1952.

† Degree of impairment based on estimate of patient's occupational and social adjustment.

Degree of Disability	Insignia
Minimal (10%)	x
Mild (20%-30%)	xx
Moderate (30%-50%)	xxx
Severe (50% or more)	xxxx

‡ Estimates of patient's verbal communication.

Degree of underverbalization	Degree of oververbalization
Slight —	+
Moderate — —	++
Marked — — —	+++

§ Psychoanalysts qualified by their respective professional societies, i.e., American Psychoanalytic Association, American Society of Adlerian Psychology, Society of Analytical Psychology.

TABLE 2.—*Status of Twelve Refractory Patients After Termination of Psychotherapy*

Case No.	Disorders *	Degree of Impairment †	Verbal Communication ‡	Length of Therapy	Type of Psychotherapy
20	Passive-aggressive personality	xxx	++	2 yr.	Ph.D.§
21	Passive-aggressive personality	xxx	— — —	1 yr.	Ph.D.‖
22	Passive-aggressive personality	xxx	— —	2 yr.	Ph.D.‖
23	Passive-aggressive personality	xxxx	— —	2 yr.	Ph.D.‖
24	Anxiety reaction	xxx	—	2 yr.	Ph.D.‖
25	Obsessive-compulsive reaction	xxxx	+++	3 yr.	Ph.D., 2 yr.‖; Psychiatrist, 1 yr.¶
26	Obsessive-compulsive reaction	xxxx	+++	2 yr.	Ph.D.‖
27	Obsessive-compulsive reaction	xxxx	— —	2 yr.	Ph.D.‖
28	Obsessive-compulsive reaction	xxxx	— — —	2 yr.	Ph.D.‖
29	Obsessive-compulsive reaction	xxxx	— — —	9 mo.	Psychiatrist.¶
30	Obsessive-compulsive reaction	xxx	— — —	6 mo.	Ph.D.‖
31	Reactive depression	xxxx	+++	3 yr.	Ph.D.‖

* For nomenclature, see "Diagnostic and Statistical Manual: Mental Disorders," American Psychiatric Association, 1952.

† Degree of impairment based on estimate of patients' occupational and social adjustment.

Degree of Disability	Insignia
Minimal (10%)	x
Mild (20%-30%)	xx
Moderate (30%-50%)	xxx
Severe (50% or more)	xxxx

‡ Estimates of patients' verbal communication.

Degree of Underverbalization	Degree of Oververbalization
Slight —	+
Moderate — —	++
Marked — — —	+++

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high incidence of obsessive-compulsive states in this series. It was our feeling that 29 of our 31 patients showed pronounced obsessive-compulsive reactions as either the primary or the secondary state.

In an earlier paper we have described in detail the reaction of our refractory group to their first experience with the common psychotherapies.[2] We based this description on the gist of what the patients themselves had to say about their initial contact with psychoanalysis or psychotherapy. This, on a purely descriptive level, is what our 31 patients reported about their first exposure to the common psychotherapies.

For the most part, these patients were quite unable to express their thoughts and feelings freely or without severe blocking. They could not expose themselves as objects of communication. Instead they used all the vehicles of communication at their command defensively or as a means of keeping their thoughts to themselves. For example, the "underverbalizers" grew ever more uncommunicative. The overproductive verbalizers merely increased the tempo of their circular, obsessional, tedious pseudocommunication.

As their first therapeutic experience progressed, these 31 patients, by and large, felt increasingly tense and fearful and developed growing signs of autonomic imbalance. Their alarm reactions — symptoms like nausea, dizziness, tension headaches, sweating, palpitation, and abdominal cramps — became ever more intense and disruptive. Meanwhile, in all but 1 of our 31 refractory cases, the doctor-patient relationship deteriorated progressively.

In not responding favorably to prolonged treatment, each of the patients in question felt, to a varying degree, that he had "failed again." His self-esteem, anything but robust to begin with, suffered accordingly. To chronic attitudes of inadequacy and self-persecution, he now added fresh feelings of nihilism and panic as to his ultimate recoverability.

By, now the large majority of our refractory group had come to associate psychoanalysis or psychotherapy with pain, humiliation, frustration, or punishment and with feelings of trappedness and hopelessness. They had become conditioned to respond to therapy as such as with an increasing fight or flight reaction. The wonder is that these patients dared to risk exposure to treatment a second time. That they did so is proof of their continued suffering and a measure of their drive toward relief from their intense feelings of loneliness and isolation.

These patients had their second or third exposure to the common psychotherapies when they began treatment with one or the other of us. During this period of one to three months of trial psychotherapy, they experienced all over again the difficulties that had defeated their first therepeutic endeavors. It appeared to us that our 31 patients were on the brink of a second therapeutic failure. At this point we therefore interrupted treatment and substituted a program of pharmacologic psychotherapy. We shall describe this program shortly. Before doing so, however, we should first like to discuss why we think that the members of this group seemed so inaccessible to the common psychotherapies.

Reasons for the Failure of the Common Psychotherapies

To begin with, how adequate was the initial contact of our group with one or another form of the common psychotherapies? All we can say is that the exposure was, in most instances, fairly prolonged and that the therapists were, for the most part, able and qualified practitioners. On the one hand, the psychoanalyses ranged in point of median treatment time of two years. The time from six months to four years, with a analysts in question were, with one exception, members of the American Psychoanalytic Association, the American Society of Adlerian Psychology, or the Society of Analytical Psychology (Table 1).

The patients in our second subgroup had had somewhat comparable initial therapeutic experience (Table 2). Their efforts at psy-

chotherapy had extended from six months to three years, with a median treatment time of two years. Their therapists, in turn, were experienced psychiatrists or clinical psychologists, all of whom, with two exceptions, had been qualified by their respective professional boards, that is, by the American Board of Psychiatry and Neurology or by the American Board of Examiners in Professional Psychology of the American Psychological Association.

In our opinion, conventional methods of treatment fell short of the mark with these refractory patients because they failed to break through a barrier that is at once psychosocial and physiologic in nature. Chief among the components of this barrier would seem to be an intense fear of any human contact, dangerously low self-esteem, attitudes of generalized anhedonia, a state of multivalence bordering on disintegration, and what may well prove to be significant, but as yet imperfectly understood, forms of physiopathology within the organism itself.

The refractory patient is handicapped in the therapeutic setting, first of all, by an intense dread of closeness. He, more than the less disturbed person, has an expectation of humiliation and rejection from any form of interpersonal contact. For him, nothing could appear much more threatening or dangerous than the prospect of self-exposure in the presence of a therapist.

The refractory patient is further characterized, we feel, by a level of self-esteem that is perilously low. His unusually sensitive antennae seem to be busy screening out ever-fresh proof of failure and inadequacy. The common psychotherapies appear to have had the effect of undermining still further the already precarious self-esteem of our refractory group.

Along with his dread of closeness and his fragile self-esteem, the refractory patient seems to qualify as a "joyless one." It would appear from a study of his life history that he has rarely experienced any sustained joy or feeling of well-being. On the pleasure-pain scale, our "joyless ones" emerged from their first two experiences with therapy feeling much the same as they had felt prior to treatment, only more so. A new type of pain and frustration—that involved psychotherapy itself—had only served to reinforce their life style of joylessness.

To do justice to the refractory patient, one must take stock of his multivalence.[3] By multivalence we mean a state of intense generalized ambivalence. The highly resistant patient appears to be riddled with conflict through and through on every level of awareness; he is torn by a multitude of contradictory responses which compete for simultaneous expression, always urgently and sometimes explosively. His oft-expressed fear of "losing control' may be a measure of the pain and anxiety induced by his multivalence. Marked polyvalence suggests a history of malevolent conditioning or of an early imprinting of highly contradictory responses. When such states of simultaneous excitation and blocking exist in extreme form, it would seem likely that no conditioning or reconditioning to new responses is possible in the usual psychotherapeutic situation. Such, apparently, was the case with our refractory group during their first exposures to treatment. The longer the process continued, whether it involved the normal procedures of free association or of vis-a-vis interaction, the closer the highly multivalent patient approached the stage of incipient breakdown.

The overwhelming anxiety, the tension and multivalence, and the distortions of thinking and feeling which inundate the recalcitrant patient must involve some form of physiopathology within the organism. Contemporary science has little more than begun to identify these psychobiological mechanisms. Whatever these mechanisms may prove to be, we are convinced that they are present, as cause or effect or both, in the evolution of all severe mental disorders, whether neurotic or psychotic in nature. Many of our highly resistant patients were so subject to "noise" or to "distortions" of central nervous system origin that they

found it next to impossible to receive or to transmit appropriate "mesages" or "information" of any sort. It is our supposition that under ordinary circumstances few therapists, however emphatic or gifted in the arts of communication, could penetrate some of these communication barriers purely in terms of the physiopathology involved.

Reviewed in this light, the failure of the common psychotherapies with our refractory group makes sense. The very exposure to therapy had triggered off a host of fight or flight reactions. It had added to the patient's nihilism and his self-mutilating tendencies. It had increased or failed to relieve his neurotic misery. The patient's psychophysiologic disturbances had continued unabated because of overexcitation of the autonomic nervous system, with resultant stress on the entire neuroendocrine system.[11] Such is the plight of the seriously refractory patient who becomes involved in the usual procedures of psychoanalysis or psychotherapy. As we see him, he is a lonely, defeated, terrified human being who reaches out for help which he rejects, for affection which he fears, and for communication which he refuses.

It seemed probable to us that our 31 refractory patients belong to a category of patients who lie beyond the reach of many of the established techniques of psychoanalysis or psychotherapy.† The program of pharmacologic psychotherapy which we subsequently initiated was an attempt to cope with the problems of these patients on two levels: first, on a psychophysiologic level with suitable pharmacologic aids, and, second, on a psychosocial level with an appropriate form of psychotherapy.[1,2]

† We can only guess at the incidence of cases of this sort. From our own experience, slightly less than one-fourth of a random series of 100 patients who were accepted for psychotherapy seem to fit our definition of the refractory case. Eisenstein reports that the incidence of "borderline" cases, from a series of 250 patients of his own, runs as high as 30%.[12]

The Pharmacologic Technique

We have described in an earlier publication the pharmacologic procedure which we evolved for the purpose at hand.[1] In essence, this technique calls for the intravenous injection of two drugs, thiopental sodium and methamphetamine. Thiopental sodium was selected for its rapid and short-acting, disinhibiting, and euphorizing effects; methamphetamine, because of its properties as a central nervous system stimulant. The effect we were seeking was a synergistic one which seemed to follow when these two chemical agents were administered intravenously in a given sequence (thiopental sodium followed by methamphetamine); at a rapid rate, and in minimum effective doses.‡

The use of minimum effective doses we found to be of crucial importance with the two drugs in question. This point was missed by most of the earlier investigators, who worked with thiopental sodium alone. The early methods of "narcoanalysis," [13,14] we discovered, produced moderate overdosage with thiopental sodium, resulting in a dazed and narcotized state; this procedure created artifacts of sedation, such as excessive abreactions and an amnesia for the interview; it impaired communication, rather than enhanced it. Even the smallest effective doses of this drug, when used by itself, tend to leave the patient in a somnolent or apathetic state, followed by a partial am-

‡ Spelled out in more detail, the procedure is as follows: Using a 10 cc. syringe, one first injects intravenously a freshly prepared 2.5% solution of thiopental sodium. In the great majority of cases 3 to 7 cc. of the drug, rapidly injected, produces the desired effect. The immediate reaction to such an injection is a loss of consciousness for a few seconds or a dazed state lasting from 30 seconds to 2 minutes. This result is accompanied by respiratory changes: an abrupt and very short period of apnea, followed by slow, shallow, and occasionally stertorous respirations. Then, using the same needle, one rapidly injects from a 2 cc. syringe 5 to 10 mg. of methamphetamine hydrochloride. The main object is to facilitate effective communication and to avoid prolonged narcotization or overexcitation.

nesia for any ensuing therapeutic experience. By means of electroencephalographic studies, we discovered that, for the purpose of expediting psychotherapy, the minimal effective dose ranges from 3 to 7 cc. of 2.5% thiopental sodium administered intravenously at a rapid rate.[1]

Likewise, with our second drug, methamphetamine hydrochloride, the smaller the effective dose the better. When administered in more than minimum effective amounts, methamphetamine produces a number of undesirable sympathomimetic effects, such as nausea, loss of appetite, palpitations, and generalized excitement, occasionally followed by states of mild to moderate depression. From our experience the appropriate dose with this analeptic lies somewhere between 5 to 10 mg., the lower limit being the preferred one. Pharmacologists in the future will doubtless produce chemical agents that are superior to thiopental sodium and methamphetamine for the purpose of facilitating psychotherapy.

The Optimal Psychophysiologic State

In response to this particular combination of drugs, the refractory patient shows a number of significant behavioral changes.[2] These changes, to be sure, are a relative matter. They vary in degree from patient to patient. The same patient reacts differently on different occasions. The response to these drugs seems to have certain common elements, however. It is these common elements which we have termed a psychophysiologic state that is optimal for psychotherapy. We shall now attempt to summarize the principal behavioral changes that our pharmacologic procedure induces in the highly recalcitrant patient.

The immediate reaction to these drugs is a brief period of somnolence. This effect lasts not more than several minutes. Thereafter, during any given interview the previously refractory patient seems to experience the following states, in varying degrees and at varying rates: a greater readiness or urgency to communicate or to expose the self in a nondefensive manner, enhanced self-esteem, increased feelings of drive and alertness, an over-all lessening of psychophysiologic tension, a greater readiness to "take a chance" on interaction with another human being, reduced multivalence, as though the patient were no longer so torn apart by his uncontrollable "yes-no" mechanisms, and, because of euphorization and anxiety reduction, the creation of a unique state for conditioning or reconditioning through reward or reinforcement.

In short, what appropriate pharmacologic intervention seems to do for the refractory patient is to create a state of altered permeability. The relatively insulated patient who responds to a psychotherapeutic situation only in terms of fight-or-flight reactions becomes more or less accessible to psychotherapy.

A suitable psychopharmacology, it must be reemphasized, is only a means of preparation for the deliberate psychotherapeutic process. The use of any ataractic drug, unaccompanied by adequate psychotherapeutic procedures, can invite disaster with the refractory patient. It can have the effect of suppressing the patient's disturbances or of disguising the warning signals of disintegration. It can also precipitate, on occasion, acute and unexpected psychotic episodes. The practice of approaching the mental patient with pharmacology alone calls to mind the inconceivable analogy of the physician who was to give an anesthetic for an "acute abdomen" without going on to perform the essential surgery.

Frequency of Treatment

The patients whose behavior we are reporting in this study had 50-minute interviews, occurring on the average once or twice weekly. As they showed improvement, we moved, not always successfully, toward the goal of using an increasing proportion of drugless interviews, until at the point of termination the pharmacologic agents could be dispensed with entirely.

Psychotherapeutic Strategies with the Refractory Patient

Once the refractory patient becomes more or less approachable due to chemical intervention, the therapist can proceed with suitable psychotherapeutic strategies. The ends and the content of the ensuing experience are the same as those of all effective psychotherapy.[15,16] The patient comes for help and for relief from his symptoms. In collaboration with the therapist, he must come to terms with his habitual distorted attitudes toward the self and others; he must be helped to understand the meaning of his recurrent interpersonal difficulties. This involves, ultimately, exploration of the patient's biography and of his current problems. If all goes well, the patient manages to substitute for his habitual anxiety-ridden modes of behavior a significant number of new ways of reacting that are less self-defeating and better adapted to the social milieu of which he is a part.

The actual psychotherapeutic operations which permit the highly recalcitrant patient to approach these ends would seem to differ in degree rather than in kind from the essentials of effective psychotherapy in general. They differ perhaps in their delicacy and flexibility, or in what must be emphasized when one is working with a patient who is so isolated and insulated, so close to the point of disintegration, and so ready to resort to fight or flight reactions at the slightest provocation. We shall now formulate in bare outline some of the strategies which we feel are appropriate for use with the refractory patient. One will note the similarity between our own approach and the technique reported by a number of other therapists who have been concerning themselves with borderline and psychotic patients.[12,17-21]

At the outset the patient for whom this form of treatment is indicated must be adequately prepared psychologically for what is to follow. We make a point of indicating to the patient ahead of time that, although he can anticipate a short dazed state at the beginning of each interview, the drugs which we propose to use are not sleep-inducing. We tell him he will then stay wide-awake and in full control of his faculties throughout the remaining portion of the interview and that he will feel somewhat more relaxed during the therapeutic hour and for a variable period following the treatment hour. Moreover, we let it be known that the forthcoming procedure entails no magic. We simply tell the patient that psychotherapy, for him, will still be a time-consuming process and that in response to these drugs he will be able to talk about the things that bother him without experiencing quite so much discomfort and anxiety. We further assure him he will be able to withhold any information that he does not wish to reveal. (Pharmacologic psychotherapy is definitely contraindicated, we feel, for any patient who shows a persistent, marked fear of the procedure.)

In all his dealings with the refractory patient, the therapist must give chief attention, first and last, to the quality and meaning of the emotional relationship that obtains between his patient and himself. The optimal psychophysiologic state only opens the door to the possibility of creating the kind of unique bond without which psychotherapy in any case is doomed to failure. Only the strongest and the most favorable emotional ties to his therapist permit the refractory patient to overcome his isolation, to work through his severe anxieties and distortions, and to relinquish his nihilistic attitudes toward life and psychotherapy. From beginning to end, therefore, the therapist must offer convincing proof at every level of communication that he is an understanding person and that he is genuinely involved with his patient and his problems. He must make the patient feel that therapy is a joint venture. He must communicate this attitude in an active way. The refractory patient must be given the feeling that he is liked and accepted, that he has worth in someone's eyes, that his therapist is interested in him as a person and is mak-

ing a sincere effort to reach him. This, we feel, is the touchstone of the approach to the refractory case. It is also the price which the highly resistant patient demands for his willingness to risk any effective continuing interaction whatsoever. On this count he differs from the less disturbed human being only in the fact that he asks a higher price and is much readier to seize on any discordant behavior on the part of his therapist as proof of insincerity, incompetence, resentment, or lack of warmth and interest.

Once the optimal psychophysiologic state and the necessary accepting attitudes of the therapist have put the highly resistant patient in a favorable psychotherapeutic climate, the problem is to keep him there. In order to maintain this state of affairs, the therapist not only must continue to show that he "cares" for his patient; he must demonstrate as well that he has the capacity to keep reacting appropriately to the constantly changing needs of the patient. This implies the establishment of a state of "oneness" between patient and therapist. It assumes that the therapist is not bound by rituals and that he can respond quickly and more or less adequately by word or gesture to whatever the patient is thinking or feeling or doing at any given moment. The type of synchrony we have in mind touches the psychotherapeutic process at every point. It affects the tempo of the treatment. It qualifies the timing, the content, and the extent of the therapist's interpretations. It has a bearing on the role which the therapist is playing or the distance which he maintains between his patient and himself at any given point of interaction.

The principle of flexibility applies, first of all, to the varying degrees of warmth or closeness which obtain between patient and therapist. Here we encounter one of the most painful conflicts of the refractory patient. This type of patient, we repeat, has an urgent need for love and acceptance. His need in this direction is equaled perhaps only by that of the schizophrenic patient. Yet he fears this sort of relatedness intensely. Consequently, he behaves erratically in the therapeutic situation. He demands closeness, and he rejects it. He advances; he withdraws; he attacks. His ability to receive warmth or to give it varies from one meeting to the next; it changes during the course of a single interview. Concurrently, the patient sees psychotherapy itself in contradictory lights: It is now a vise, then an attack; now an approach to freedom and independence, then an experience involving "brotherly love" as Eric Fromm uses the term. Nothing would seem to contribute more to the eventual growth and recovery of the refractory patient than his discovery that he can move toward another human being—his therapist to begin with—without being humiliated or injured by the experience. The chances of his making that discovery are greatly reduced in our opinion unless his repeated testing operations in this direction are responded to in a synchronous manner, that is, by a therapist whose readiness to exchange warmth and affection within therapeutic bounds matches but does not exceed, at any given moment, the limits which only the patient himself can set. To facilitate this sort of interaction, we believe that the therapist should sit where he can see the patient and where the patient can see him in return. Thus both patient and therapist can take full advantage of nonverbal as well as verbal cues.

The same flexibility should govern the strategies of the therapist on the level of insight or interpretation. The therapist must take special pains to adjust to the patient's own pace and to the patient's own tangential approach to his problems. He must know when to be active and when to slow down. Here, again, the refractory patient has powerful contradictory needs. He is groping urgently for certainty; he requires simple, frank, credible formulations. Moreover, the dynamics of his case crystallize out, both in his own mind and in his therapist's, much more quickly during pharmacologic psychotherapy than during "ordinary" psychotherapy. At the same time, as Freud warned us, the therapist must exert no pressure in the

form of "wild analyses" or premature insights.[22] Such pressure would only serve to increase the patient's already dangerous state of multivalence. Once more the therapist must rely on his own empathic and intuitive powers.[18] He must gently feel his way into the anxiety-charged areas of the patient's life. He must carefully percuss the tender areas, so to speak, allowing the patient to release no more anxiety than he can safely absorb at any given time. Certainly, the therapist's interpretations should be sparing and meaningful at all times. Mere interrogation of the patient must be guarded, especially during the early stages of pharmacologic psychotherapy. Again, on grounds of multivalence, the therapist who works with refractory patients must avoid the use of free association. He must also steer clear of making psychotherapy an obsessive seeking after memories. The therapist who ignores this point may succeed in maintaining his own security or in bolstering some of his own favorite theories, but, in doing so, he may upset the patient's precarious equilibrium.

If patient and therapist continue to interact in a synchronous manner, they prepare the ground for what appears to us to be, essentially, a suitable milieu for new conditioning or reconditioning.[19] The patient, for his part, begins to experience a whole series of rewards or satisfactions in the therapeutic situation.[2] He tends to respond with mounting pleasure to the experience of feeling accepted and understood, to the gradual release from unbearable psychic and physical tension, to the fact that he can test out his relatedness with another human being without fear of retaliation. As his immobilizing multivalence begins to dwindle, he enjoys the feeling of freedom, the fact that he can act or make choices without panic or devastating anxiety. He is further rewarded insofar as a kind of order or meaning replaces bit by bit the previous discord and chaos of his inner life and his interpersonal world. Not the least of these satisfactions—and one of the striking phenomena of pharmacologic psychotherapy—is the increased degree of the patient's participation in the psychotherapeutic experience. As he tests out the situation and finds it tolerably safe, the highly resistant patient, with expected variations from person to person and within the same person, leads the way time and time again to the sources of his misery. Despite the pain involved, he seems to delight in the process. He reacts much the same way when his therapist arrives at some formulation that is timely or seems to ring true. Our concept of what is happening at this point is this: The "excommunicated" one is beginning to experience the joy of communicating intimately and meaningfully with another human being, perhaps for the first time in his life.

By virtue of the lessened anxiety and the enhanced drive and alertness that follow from the drug-induced state, the refractory patient is better able to "work through" his difficulties in prolonged psychotherapy. Mere interpretation and insight, however valid, are never therapeutic in and of themselves. The "working-through" process is all the more crucial and prolonged with the refractory patient. The goal is, first, the evolution of a more or less constant group of new and more appropriate attitudes toward the self and others, and, second, the extinction of a host of inadequate disabling responses. The attaining of such a goal, particularly with the highly resistant patient, is at best a slow and difficult learning process. No refractory patient can stick it out or benefit from the process, in our opinion, unless he experiences the rewards and satisfactions of the psychotherapeutic situation over and over again for an extended period of time.

It would seem to be the slow accumulation of such satisfactions that makes psychotherapy effective in any case, particularly with the patient who is highly inaccessible. Lacking these rewards, the refractory patient cannot face the hazards that psychotherapy involves, nor will he permit anyone to break through the protective barrier that

separates him from the outer world. It is our view that if the extremely recalcitrant patient is to succeed in extinguishing a significant number of his manifold anxieties, if he is to endure the long process of "working through" his many difficulties, if he is to share at all fully in the experiences of identifying and correcting his distorted attitudes toward the self and toward others, the pleasures and the rewards which he experiences in psychotherapy must ultimately outweigh the pain.

This is not to imply that pharmacologic psychotherapy at its best does not have its interludes of stress and anxiety for both therapist and patient. This procedure would have no point if its aim was only that of producing what Aldous Huxley described in his volume on mescaline as "chemical vacations from intolerable selfhood." A pharmacologic psychotherapy without adequate psychotherapy runs this risk, among others. It could lead to various states of habituation or dependency. The patient could come to enjoy the "optimal psychophysiologic state" for its relaxing effects alone. Anxiety, we are aware, is the very fulcrum of mental illness and of the psychotherapeutic process. Without the presence of this feeling state in some degree, life itself as we know it would be meaningless. In the psychotherapeutic situation, anxiety provides the impetus and opportunity for change; its magnitude is the index of the severity of any given disorder; its management decides the success or failure of all psychotherapeutic efforts. Our aim is to limit its severity so that it becomes bearable. Only then, as we see it, does the markedly refractory patient become "open" to new learning or new conditioning.

Our psychotherapeutic strategies are not directed solely toward the treatment room. From the inception of treatment we try to utilize the same "working-through" process so that psychotherapy or psychotherapeutic tenets do not become a substitute for life. If the refractory patient is to realize any of his potentialities as a human being, he must sooner or later become involved with living itself with all the courage and all the maturity that he can command. For him, as for any other type of patient, therapeutic success does not consist of his "conversion" to any particular psychotherapeutic credo or of the acquisition of an obsessive or a terrifying new vocabulary, from which his friends and relatives are forced to take flight out of awe or fear or sheer boredom.

To a humbling degree, the psychotherapist who works with refractory patients must keep alive his own resources of altruism and emotional maturity. This means that he must himself both understand and resist many of the dehumanizing pressures within the world around us. He must see his patients not just as "minds" or "nervous systems" or "states of unconsciousness" or merely as sources of income or prestige, but as lonely, suffering human beings who are calling out to a fellow human being for help. To remain worthy of his role the therapist must pay heed to Eric Fromm's reminder that "man is not a thing."

Results of Treatment

Our estimate of the final outcome of treating refractory patients with pharmacologic psychotherapy leaves much to be desired.[28] It is couched, to begin with, in terms of the subjective "categories of impairment" proposed by the Committee on Nomenclature of the American Psychiatric Association.[4] By improvement we mean that a patient is able to reach and to maintain a somewhat better life adaptation: an enhanced capacity for productive work and certain changes in interpersonal behavior which both the patient and those with whom he is in regular contact find more or less satisfying. With disorders of long duration and of the type of severity which we are considering, it follows that our therapeutic goal was one of achieving, whenever possible, relatively durable states of amelioration.[16] Now for our tentative findings.

After fairly prolonged treatment, roughly one-fourth of our patients (22.6%) made

TABLE 3.—*Status of Nineteen Refractory Patients with Previous Psychoanalysis Following Pharmacologic Psychotherapy*

Case No.	Disorders	Length of Treatment	Extent of Impairment		Degrees of Change
			Before Treatment	After Treatment	
1*	Passive-aggressive personality	3 yr.	xxxx	xx	++
2*	Passive-aggressive personality	1 yr. 4 mo.	xxxx	xx	++
3	Passive-aggressive personality	2 yr. 6 mo.	xxx	xx	+
4	Passive-aggressive personality	2 yr.	xxx	xx	+
5	Passive-aggressive personality	1 yr. 2 mo.	xxx	xx	+
6*	Passive-aggressive personality	1 yr. 3 mo.	xxxx	xx	++
7*	Passive-aggressive personality	2 yr.	xxxx	xx	++
8*	Passive-aggressive personality	2 yr.	xxxx	x	+++
9*	Passive-aggressive personality	1½ yr.	xxx	xxx	—
10*	Passive-aggressive personality	1½ yr.	xxx	xxx	—
11	Passive-aggressive personality	1 yr. 7 mo	xxx	x	++
12	Passive-aggressive personality	6 mo.	xxxx	xx	++
13*	Obsessive-compulsive reaction	3½ yr	xxx	x	++
14	Obsessive-compulsive reaction	1½ yr	xxxx	xx	++
15*	Obsessive-compulsive reaction	4 yr.	xxxx	xxx	+
16	Obsessive-compulsive reaction	1 yr. 7 mo.	xxx	xx	+
17*	Anxiety reaction	4 yr.	xxx	xx	+
18	Anxiety reaction	1½ yr.	xxx	x	++
19*	Schizoid personality	2 yr.	xxxx	xxxx	—

* Discharged.

no progress whatsoever. One-third of our patients (32.2%) improved to a "slight" degree; they moved from one level of incapacitation to the next less serious level of incapacitation. Slightly more than a third of our total group (38.7%) showed a "moderate" degree of amelioration; they moved from one category of impairment to a less serious category of impairment two steps removed. A handful of our patients (6.5%) registered "considerable" improvement; they moved from the most serious to the least serious level of disability. Slightly less than one-half of our patients (45.2%) made significant improvement, that is, "moderate" to "considerable" gains. The sign test reveals that these changes, taken at their face value, lie beyond chance.[23]§

Table 3 and Table 4 present our findings in a more detailed form.

It will be noted that our treatment situations were prolonged in character. The length of care extended from six months to five years, with a median treatment time of two years. It follows that pharmacologic psychotherapy, as we have employed it, is not to be equated with brief psychotherapy.

The lasting quality of these estimated changes is another question. Here it would seem much too early to risk final judgments of any sort. Of the 31 members of our refractory group, 16 have terminated treatment. So far as we can determine, these 16 patients have held their gains; they have been able to function on their own more or less successfully—within the limits which we have emphasized—for periods of time ranging from one to three and one-half years. These are fragile human beings, however, who are unusually susceptible to stress. We anticipate, therefore, that a certain number of our group will require some form of occasional or intermittent psychotherapeutic help for the rest of their lives.[24]

What we should prefer to accent at this juncture is neither magnitude nor the durability of any of the therapeutic gains which may have occurred. Our primary object is, instead, to call attention to a specific pharmacologic and psychotherapeutic technique that opens the possibility of effective psychotherapeutic interaction and of melioristic gains for patients whose disabilities might otherwise remain, for all practical purposes, irreversible.[16]

§ If the seven "no-change" cases are counted as negative instances, the difference in favor of improvement is significant at the 0.01 level of confidence. If the "no-change" cases are classified as ties, the difference in favor of improvement lies well beyond the 0.01 level. These statements of probability rest, of course, on the assumption that our underlying clinical observations represent "good" data.

TABLE 4.—*Status of Twelve Refractory Patients with Previous Psychotherapy Following Pharmacologic Psychotherapy*

Case No.	Disorders	Length of Treatment	Extent of Impairment		Degrees of Change
			Before Treatment	After Treatment	
20	Passive-aggressive personality	2 yr.	xxx	xx	+
21 *	Passive-aggressive personality	2 yr.	xxx	x	++
22	Passive-aggressive personality	1 yr.	xxx	x	++
23 *	Passive-aggressive personality	2 yr.	xxxx	xx	++
24	Anxiety reaction	4 yr.	xxx	x	++
25	Obsessive-compulsive reaction	4 yr.	xxxx	xx	++
26	Obsessive-compulsive reaction	1 yr.	xxxx	x	++
27	Obsessive-compulsive reaction	5 yr.	xxxx	xxxx	—
28 *	Obsessive-compulsive reaction	2 yr.	xxxx	xxxx	—
29 *	Obsessive-compulsive reaction	1 yr.	xxxx	xxxx	—
30	Obsessive-compulsive reaction	3 yr.	xxx	xx	+
31 *	Reactive depression	1 yr.	xxxx	xxxx	—

* Discharged.

Comment

As we have indicated physiopathology may account for much of the rigidity and seeming irreversibility of many of the severer forms of psychoneurosis and personality disorder. We should now like to speculate on the nature of this physiopathology. It is here, we feel, that one may have to turn in order to appraise the response of the refractory patient to psychoanalysis and the common psychotherapies, on the one hand, and to pharmacologic psychotherapy, on the other.

We are impressed, first of all, by the apparent irreversibility of the learning process which Liddell and Blauvelt [5] have reported from their experimental study of animals. In order to enjoy a normal course of development, according to these investigators, the newborn kid must live through a number of appropriate or synchronous early experiences with the mother goat. If these experiences do not occur in the proper sequence during the first few hours of life, on the other hand, the kid is doomed. Whatever happens to him from then on in the laboratory or in the pasture, he remains to the end of his days a markedly disturbed, biologically inferior specimen. As a matter of fact, this state of dysynchrony between the newborn kid and the mother goat may lead to the young animal's early death.

Similar observations on the irremovable effects of early conditioning come from what the ethologists Tinbergen and Lorenz [6,7] have to say about imprinting in birds. These observers define imprinting as conditioned responses which occur very early in the life of the bird. Once learned, such responses are fixed and unerasable. They give way to no new conditioning in these areas, however necessary or favorable this new learning may appear to be from the standpoint of the survival of the individual or the species. Thus in the laboratory birds can be imprinted for mating activity directed toward the human experimenter. They will thereafter attempt to consummate this substituted sexual activity, ignoring any subsequent favorable opportunities for mating with members of their own species. Lorenz draws a parallel between this rigid sort of conditioning and the behavior of some of the human fetishists whose life histories he encountered in the pages of Kraft-Ebbing.

We owe to the ethologists the description of another related mechanism that may add something to our understanding both of psychopathology and of psychotherapy itself in humans. This is the biologic, rather than the psychiatric, mechanism, to which the science of ethology has given the label "displacement activities." By displacement activities the ethologist has in mind various forms of inappropriate, substitute behavior that occur when a powerful drive is thwarted or when two equipotent competing drives are activated simultaneously and neither can find direct release. These substitute or displaced activities, when they occur, appear to be extraneous or irrelevant or "out of context." They arise, say the ethologists,

when the undischarged energy of the thwarted or competing drives "spills over" into other, unrelated physiologic or behavioral systems. It is the conjecture of both Lorenz and Tinbergen that a good deal of psychotic and neurotic behavior may involve imprinting and conditioned displacement activity. Be that as it may, instances of such imprinting and displacement activity abound on the animal level; they are signals of conflict; they are learned early in life through repeated conditioning, and, once learned, they can become relatively fixed.

In search of models that help to explain our own data, we, in turn, see a relationship between the observations of Liddell, Tinbergen, et al. and certain cybernetic concepts. One can postulate that displacement activity in particular involves a disturbance of "reverberating circuits" or a break in the "negative feedback system" of a complicated servo-mechanism. Thus, instead of proceeding from A to B to C, and eventually to goal X, the conflicted organism fails to reach goal X but moves instead from A to B to C, thence back again to A, in a never-ending circle.

Some portion of the psychopathology of the refractory patient we would attribute to imprinting and to the operation of conditioned displacement activity. That is, when the severely disturbed, anxiety-ridden patient becomes immobilized by his multivalence, when his multitudinous competing drives are denied expression, when he becomes more and more incapable of goal-directed behavior, his undischarged energies overflow into "irrelevant" areas. This energy appears in the form of compulsive and obsessional trends; it overflows into one or another somatic system; it shows up as disturbances of communication or as autistic or dereistic thinking; it ends in self-destructive and self-multilating behavior. From the standpoint of psychotherapy, these pathologic displacement activities have this importance: They are learned; they are reinforced by chronic anxiety and multivalence; they contribute to the physiopathology of psychosis and severe neuroses. Their existence helps to explain both the panic and the immovability of the refractory patient when one tries to reach him by way of the common psychotherapies.

It is this more or less rigid physiopathology that would seem to give pharmacologic psychotherapy its basic rationale. Our own procedure is, in one sense, a method of attacking the physiopathology of the organism in such a way that the path can be cleared for psychotherapy. It is our supposition that thiopental sodium[25] and methamphetamine may act on the ascending reticular system described by Magoun and his group of investigators. In any event, thiopental sodium seems to muffle the patient's anxiety mechanisms. This drug, together with the alerting and driving action of methamphetamine, appears to have the effect of reducing, temporarily, the dominance of imprinting and conditioned displacement activity within the organism. It is at this point that the therapist achieves a break-through in the psychopathologic barrier. So long as this state persists, the broken, "reverberating circuits" of the "negative feedback system" are partially restored; the competing responses of multivalence are stilled; patient and therapist can establish effective lines of communication, and the patient can participate in the long learning process that is required for the acquisition of new and more appropriate behavior and for the extinction of his inadequate and disabling repertoire of responses.[26] Under such circumstances, it has been our experience that the refractory patient can acquire in time a stable group of new and more appropriate behavior patterns and that these patterns carry over from the treatment room to life itself. These gains by no means constitute anything like total reconstruction for the refractory patient. But they do seem to permit the patient to make a significantly better life adaptation.

It is said that Sullivan[19] and a number of other notable therapists[17,18,21] who worked with borderline and psychotic cases have been able to perform "curative feats" through

psychotherapy alone. We do not doubt that psychotherapists of this order possess incredible intuitive and emphatic powers. But we ourselves have never been able to effect significant and lasting positive changes with severely refractory patients when we relied solely on the conventional arts of psychotherapy. Other qualified therapists with long experience apparently had the same difficulty with our group of 31 refractory patients. The fault may lie with ourselves. The psychotherapist with something less than extraordinary talents may simply lack the art of breaking through what appears to us to be, with the highly refractory case, the insuperable barrier of physiopathology. It is our respect for this barrier that leads us to suppose that pharmacologic psychotherapy shows promise of becoming a treatment of choice with some of the severer forms of psychoneurosis and personality disorder.

Summary and Conclusions

This paper concerns itself with a group of 31 refractory cases. All of these patients were suffering from severe psychoneuroses or personality disorders. All had failed to respond favorably to previous psychoanalysis or psychotherapy. We attributed this failure to the existence of an all but impenetrable communication barrier, which appeared to be at once psychosocial and physiologic in character. In order to breach this barrier, we produced an optimal psychophysiologic state for psychotherapy by using two pharmacologic agents, a thiobarbiturate and an analeptic drug. This procedure seemed to open the way for effective new conditioning or reconditioning. The ensuing psychotherapeutic strategies differed from the common psychotherapies only in degree; they involved greater delicacy, a longer and more painstaking process of "working through," and greater attention to the creation and maintenance between patient and therapist of a close, synchronous, and flexible relationship. Approximately one-half of the 31 members of our refractory group showed a significant and relatively durable improvement. Our experience leads us to conclude that two procedures are definitely contraindicated for the refractory patient: (1) any form of psychopharmacology unaccompanied by an appropriate type of psychotherapy, and (2) exposure to psychoanalysis or the common psychotherapies as these arts are currently practiced. For the type of patient we are discussing, such treatment methods can be a damaging or disintegrating experience. Pharmacologic psychotherapy, on the other hand, shows promises of becoming a method of choice for the treatment of some of the severer forms of psychoneurosis and personality disorder.

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Expressive Form in Schizophrenic Language

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In the course of ordinary experience, certain assumptions implicit in the use of language allow for a smooth, flexible transaction of daily affairs. Language is expected to communicate rational thought. This postulate, indispensable to the intent or purpose governing the use of language, may shift imperceptibly to attach to language itself. Language, as a concept, is often treated as synonymous with communication or with logical thought.

Communication, and the transmission of intelligible meaning, are values perceived in language and assigned to language. The schizophrenic patient's language meets these criteria only imperfectly. Under these conditions it may be of value to examine language within a wider range of its functions and operations.

For the therapist, "understanding" the language of a schizophrenic patient often involves a capacity to empathize with the patient and, by a process of identification, to unravel the complex meaning of the symbols used. The words then become intelligible by virtue of a different value assigned to language, namely, its role as a process of symbolic transformation. In terms of function alone, the processes of symbolizing, of giving form and order to the apprehension of reality, of mediating and molding the perception of reality, of selecting and defining the content of reality, become accessible as instruments through which to investigate the nature of mental processes. This area can broadly be designated as an aspect of language having to do with the *representation of reality*.[1] Language can also be seen as a *record of past experience*.[2] In the individual, as well as in language communities, acquired contextual referents, modes of association, nuances of expression, sematic levels of abstraction and conceptualization, trace the acquisition of intellectual and ideational habits throughout a lifetime. Language possesses yet another facet, not generally acknowledged in scientific approach. Language can be perceived as an *expressive form* which bears the imprint of the individual.[3]

The general notion of expressive form, as an element identifiable in man's creative activity, has been transferred from the context of aesthetics to reappear in the context of psychology as "expressive behavior."[4] Expressive behavior is broadly defined as the reflection of the individual's more stable and consistent traits within the form and pattern taken by his action or production. Language is an integrated, complex activity by which form and expression are given to mental events. It adapts easily to the characteristics of the speaker, as well as to content. This quality gives language great psychological value. Linguistic patterns, considered as a form of expressive behavior, appear to show consistencies with psychological patterns.[5]

The phenomenon of style, the question of the "how" as well as the "what" of things, is often relegated to the sphere of "intuitive" appraisal and impression. However, when "style" is placed within its proper context as a part of the general expressive behavior of the individual, it lends itself to more orderly and transmissible observation. Although intractable to strict analysis, interpretations can be made with objectivity and judgment that lift it from the level of subjective impressions to one of exposition and criticism.

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The exposition which follows is an attempt to view a schizophrenic patient's language as an expressive form in which the observable characteristics of language are used as indices to the psychological characteristics of the individual.

Language Pattern

The accompanying text is a verbatim transcription of a schizophrenic patient's language. This specimen is obviously illustrative, rather than inclusive, but stands as being representative of her general style of discourse. For distinctness, the predominant patterns, as shown in the language behavior, are isolated in the two paragraphs. The interweaving of these patterns in actual discourse is indicated by the dotted lines. Illustrations with a running commentary are given in order to show the derivation of psychological interpretations.

The interviewer commented that a long time had passed since seeing the patient, and perhaps they might chat.

"I haven't time to live my life. I have not the time. Fifty years is a long time. It is a century. I hear you have a new school off the Florida key; you planted a lantern. That is a key. It seems to me it was about twenty years ago we planted the lantern that's a key. There is a question I was asked, who, who planted the lantern that's a key? Transmit (interviewer puzzled). Dense, Hortense. How many seconds on a thousand islands is another question I was asked. Equal the two. I think I am playing regret. There was a walk, a brick walk. I don't know where it is gone. Well, there was a step of white marble and a magenta walk and that is all. It led to no palace. Well, that is regret. Danger field . . . . Chitchat. You can chitchat, you think. All right, whenever you chitchat, you think. All right, you have shown me. Contraction . . . She always had the last word from the fountain. (Of wisdom?) Aerial up. Well, I'm not sure of the wisdom. Wisdom is not always chic. The point made. There was a question of holding the point at what level. The question of holding the question with one point, with another point, and with another point. The point was doubtful. With or without.

. . . . "Regret. Where is Rita. Rio Rita. *Pas regrette. Regrette.* No. Rita. The infanta. Same as Rita. L'Infanta and Rita, the same. Velasquez. Line is. You said us, I believe. No. Why is. Gold leaf. English maple. In a breeze. Have another cookie. The children get two. The children get into. *Difficultés des vieux. Difficultés des jeunes.* Day and noo-it. Noo-it and day. Compact powder. Caron, Contraction . . . . I thought New York too small to hold. One expands from tree to tree. Dryads. Seven Druids. Celts. The Celts of 5th Avenue. Wall Street, the street of kings. C Street. The stand is the sea. Eva. That is Siva. S-E-A."

The language pattern roughly divides itself into two major trends: There is a drift toward structured, syntactically correct expression of ideational content, although the sematic implications are in the main obscure (first paragraph). The second trend (second paragraph) is a drift toward fragmentation of structure and syntax, notably a dropping out of the relational, form-giving elements of language, so that a naming of objects, events, qualities predominates.

The first pattern is one that carries ideational import. The discursive propositional function of language is intact. The flow and threat of an underlying meaning can be discerned in the familiar formal relationship of statements. The meaning is left implied, open to interpretation. This gives to the patient's language that elusive, suggestive quality which points to meaning by giving it form, but fails to complete the gesture by providing the appropriate content. It derives from the fact that the words which ordinarily carry designative, referential meaning are used instead on a symbolic level. A shift in context occurs in which the symbolic function of words is substituted for the referential or sign function of words.

The patient shows a tendency to symbolize her inner experiences and awareness in imagery. Metaphor is repeatedly used to express an idea. Elsewhere she refers to herself as a "deflated balloon that will not inflate again"; to her therapist at various times as "standard bearer," "medium," "dictator." This figurative approach suggests something of this patient's original imaginative endowment. Further support is given to the notion that this patient thinks easily in metaphor and analogy by statements such as the following: "We've not seen you for

a long time. It is almost as bad as the sunshine." The idea conveyed is quite clear. In it is contained, in a comprehensible fashion, the same tendency which emerges in an incomprehensible fashion when the analogies or metaphors are more personal and private. Occasional meaningful statements such as these suggest that the mode of symbolizing through imagery is a characteristic of the patient's habitual mode of thought.

This mechanism is a familiar one in another area, where the expressive function of language, rather than its communicative function, is in the foreground. In poetry concrete images are often used to express a condensed meaning. But here the similarity ceases. Poetry employs images as symbols to illuminate and intensify meaning. The schizophrenic patient frequently used images as symbols on a capricious and arbitrary basis to deflect meaning. "Key," "lantern," "a walk," "castle," as used by the patient, become a metaphor because of an assigned meaning, rather than an implicit one. As a result, the language pattern begins to show marked characteristics of transposition and substitution. It begins to approximate a code or a cipher. These statements of transposition and substitution read like a cryptogram: "I think I am playing regret. We have lost the walk, a brick walk. I don't know where it is gone. Well, there is a step of white marble that is a walk and then there is a magenta walk and that is all. It led to no palace. Well, that is regret." If the appropriate referent were substituted for the key word, a meaning might emerge. "I think I am playing. . . . We have lost . . ., a . . .; I don't know where it is gone. Well, there is . . ., and then there is a . . . and that is all. It leads . . ., well, that is . . ." might conceivably translate into "I think I am feeling regret. We have lost a habit of talking, a way of communication; I don't know where it is gone. Well, there is your way of talking and there is my way of talking and that is all. It leads nowhere. That is regret." The meaning is lost to the listener who does not possess the code. This tendency toward verbal puzzles is further compounded by the recurrence of overtly expressed riddles: "How many downs to a touchdown? —who planted the lantern or the key? —how many seconds on a thousand islands?" Implied and disguised meanings run through all of these statements. In addition, there are many terse, pointed punctuations relevant to the speaking context and focusing deliberately upon the perspicuity of the listener: "Contact" . . . "Transmit" . . . "Dense—Hortense" . . . "Aerial up—aerial down"; "Equal the two"; "danger field." The focus upon riddles, substitution, transposition, and the direct notation of the listener's ability to decipher meaning, shift the interview from one of overt expression to covert expression, with implied invitation, challenge, or solicitation to enter the patient's private world of meaning.

The function of ciphers, codes, and puzzles is to disguise meaning, and yet they are meant to be deciphered. They serve to interest and intrigue. If these elements of disguise, intrigue, and double intent of concealing and revealing are prominent in the pattern given to language, it seems likely that these same elements have their source as prominent characteristics of the speaker. A double purpose suggests ambivalence. Further, if language is not permitted to perform its usual task of communication demanded by the situation, it may take on some other function. In this instance, language is being manipulated to structure an interpersonal situation. The speaker then appears as a person who subordinates convention and authority to her own wishes.

However, the excessive and complex use of disguised meaning, riddles, and verbal play, the inflexibility of this mechanism, suggests a habit that is no longer under the controlled direction of the patient, but continues at its own pace. Automatisms can be set up in psychological spheres, as well as in motor and behavior spheres.

The second trend (second paragraph) taken by the language pattern is one of fragmentation. Elements (words, phrases) stand out in isolation. Connections, transitions, relationships are not given form. There is no evidence of ideational continuity, no evidence of a context within which the assorted words and phrases take their proper position. One determinant of language is displaced by another: Talking "about" something, the expression of ideas, gives place to the speaking "of" something, a naming of objects, events. The relational, dynamic form underlying a process of thinking gives place to a static structure, objects of thought.

This abrupt transition from one level of language use to another implies a shift in mental operations from one level to another. Language no longer functions as communication, or even as expression of mental events. It is at this time more correctly described as an "activity."

This second level of language has no apparent semantic continuity. It has, however, a continuity at associational and perceptual levels. Each referent appears to act as a stimulus to one or more associations: "L'Infanta . . . Velasquez; gold leaf . . . English maple . . . breeze." "Dryads . . . Druids . . . the Celts of 5th Avenue . . . Wall Street, the street of kings. C Street . . . the stand is the sea." The general laws of association—contiguity, continuity, comparison, contrast—can be discerned. Another associational level comes into play which appears determined by sensory qualities, such as the sound of the word (street—the sea; children get two—children get into; line is—why is) and a feeling for repetition and rhythm (*difficulté des jeunes;* day and noo-it, noo-it and day). Guiding principles of rhythm, rhyme, and balance determine the connections. Words apparently are treated as percepts, with qualities such as sound and rhyme, rather than as semantic units. Words become objects with which a variety of operations can be performed: New combinations are made; rhyme and rhythm are imposed; repetition occurs. The manipulation of language at associational and perceptual levels, with disregard for the semantic value of language, is often noted in manic patients. It is also familiar in the prattle of children, and in adults when in a hypnagogic state. The similarity and continuity of behavior patterns demonstrate basic psychological patterns deeply rooted in human nature. Automatisms of repetition, rhythm, symmetry, and balance can impose themselves on as highly a differentiated and specialized a medium as language.

In this second distinctive pattern the inconsequential flow of images and notions has something of the quality of free association. The patient appears highly receptive to stimuli at the level of impressions and percepts. These are registered singly and are not related by reflective thought or placed within a meaningful context. Associations seem to be carried along on an impressionistic basis. One image suggests another: dryads—Druids—Celts.

The universe of discourse shown in this language pattern is extensive and varied. A great number and variety of subjects are touched upon. The references to exotic places, to peoples, real and imaginary; allusions to the world of art, literature, the world of movies and popular songs, to games, snatches of foreign languages, quotations, suggest a lively mind that noted and registered its exposure to both an actual and a cultural environment. Different levels of awareness are tapped—the concrete, the imaginary, the abstract, the conceptual. There is a tendency toward particular notation, differentiation of impressions, as opposed to generalization or fusion. The correct use of abstract terms (transmit, contact, casual, expands, reverse, regret) indicate a potentially high intellectual level of operation. Certain words used in self-reference (I marvel; I admire; I . . . elusive) suggest a fine discrimination of attitudes and qualities. All pronouns are woven into the language pattern. "I" is given very minimal stress, suggesting that the flow of talk is not self-observant or self-conscious but spontaneous.

Statements which indicate inferential reasoning are notably absent. The sentences are in the main declarative, rhetorical, descriptive, and exclamatory. Connective words of a logical order—"if," "then," "but," "because," "therefore"—which ordinarily show the steps of reasoning, are rare or absent. This suggests that the patient deals with intuitive perceptions, less with the processes of inference and causal relationship, with systematization and ordering of ideas.

An important point noted is that the transformation of idea into image and symbol in continuous. New symbols are created to encompass new meanings, new situations. To create meaningful and appropriate metaphors requires an ability to abstract and to synthesize abstractions into new patterns. This appears as evidence that the mental operations of abstraction and conceptualization do occur.

The nature of the images, as shown in metaphor and analogy used, is informative. Where the patient's meaning is discernible, these figures of speech are in the main clear and precise, rather than loaded with condensed meaning or ambiguous. There is little doubt as to the meaning of "medium" or "standard bearer" as used in reference to the therapist. Meaning, when used overtly, is made explicit rather than implicit. This suggestion of an orientation toward clarity and precision is also noted in neologisms, such as "psychoanalytizations," used in reference to therapy. Meaning is compressed into an apt or pointed phrase, not fused.

The patient manipulates her verbal tools with some sophistication and skill: "Chitchat. You can chitchat, you think. All right, whenever you chitchat you think." "Well, I guarantee not to help, but I get the point. The point made is a point. There is a question of holding the point. A question of holding the point at what level?" This play upon words and regard for intellectual nuances suggest a mental alertness and cleverness, with some liking for display of verbal, intellectual sophistication.

As to tempo, a grace and charm is manifested in her language. It is not stereotyped or static, but quick, uneven, varied. Short, staccato words and phrases mingle with longer, more evenly flowing sentences. This suggests a restless temperament, capable of serenity but never phlegmatic or monotonous.

This patient appears capable of using language only at extreme levels: as an automatic activity, or as a subjectively overdetermined, highly individualized, intellectual performance. A whole world of intermediary adaptation to communication or expression, the entire area of denotation, goes unrecognized.

This language pattern is characteristic of a "chronic schizophrenic" woman, hospitalized for the past 30 of her 50 years, isolated, withdrawn, delusional, and hallucinated. Since the early years of her hospital admission, she has carried on a highly individualized pattern of speech.

Fortunately, this patient's hospital record contains some vivid reproductions of her language habits of 20 years ago. They were made at that time by her therapist, who, in working with this patient, developed a high degree of accuracy and skill in interpreting her meaning. Some excerpts from the record of 1938 are quoted below:

"If you grab in the grab bag, then what you grab is taken away from you."

"If you have a little mound and build it up and up and up, and then someone comes along and says, 'I would rather sit up there,' and so you are pushed off and rolled down and down and down."

"You can use my thoughts outside."

(I once asked her if she had a pleasant weekend and got the expected intimation that her life is not pleasant at all. Then she said: "What would it take to spend three years and $25 to see?" She implied, "What would it take to interest you to this degree?")

(She referred to the examiner as "an experienced standard bearer," who was used to helping people.)

(When we talked about her outlook for the future, she said, "The balloon is flat. It cannot be inflated or deflated.")

(She would like me to control her, to "give her the line" and "pilot the ship.")

(The patient feels that I understand her—"talk her langauge.")

(When one brings up the question of her own wishes, she evades, saying, "I am not in the case.")

In taking a longitudinal view of the language pattern through this span of years, some interesting features present themselves: Twenty years ago the patient's language showed the same dominant characteristic of simultaneously revealing and disguising her meaning by substituting concrete imagery for concept and idea. Yet the schism between her personal, individual frame of symbolic reference and the conventional frame of symbolic reference was not so wide. Communication, a sharing of a mutual frame of reference, was quite possible if the other person showed a readiness to translate and interpret. With passage of time, with an isolation and intensification of one habitual mode of thought and speech, with no one to interpret, to translate, the distance widened between personal imagery and more universally recognizable imagery.

The patient's mode of handling meaning in language appears to have undergone interesting transitions. The initial predisposition was one of converting and condensing meaning into an image. By 1953 (as shown in the excerpt used for analysis) this mode had developed toward franker disguise and concealment of meaning in an image. In 1957 a further development appears, namely, the avoidance of meaning by clinging to the literal interpretations of a statement or perceptual facet of a word. Repeatedly when asked a question, the patient answers in a literal sense:

("What does it mean . . . Don't cry over spilt milk?)

I did today.

(What happened today?)

Today happened today.

(To what aim do you refer?)

I do not refer; fur is . . . fur is a cover for the animal kingdom.

In the last question and answer particularly, one sees the beginning of a habit which may eventually crystallize into the so-called "concreteness" of schizophrenic language. The preceding notation, "I do not refer," shows that in negating the conceptual meaning an awareness of the conceptual implication exists. Resorting to a *Klang* (percept-linked) interpretation is here still a patent denial or avoidance, but not lack of awareness, of the meaning of "refer." If presently, from indifference or habit, the denial drops away from such statements, the answers will indeed appear "concrete."

It raises the question whether schizophrenic "concreteness" in this instance may not represent less an inability to abstract than a defensive or an avoidance reaction to the meaning behind words.

This retrospective glance shows the strong stamp of a language style that appears indelibly her own, a style of language that represents the patient's mode of perceiving and responding to reality. The rich use of imagery to express meaning has undergone transitions based on feelings and needs: to express→ to conceal→ to avoid. In time these habits become fixed and discernible in the language pattern.

Interpretation

As one summarizes the features that can be identified in the form and pattern of language, the following interpretation is made: On the one hand, language partakes of the qualities of a cipher, a continual process of transformation and translation of privately recognized meanings into suggestive, but disguised, verbal symbols. This in itself is an intellectual act that requires the mechanism of ideational thinking, such as abstraction, conceptualization, symbolization. It argues that the formal mechanisms of intelligent thinking are accessible to the patient. This is further borne out by the intact syntactical structure of these statements, which bear witness to the persistence of logical and orderly disposition of her ideas.

On the other hand, a great part of the language pattern appears to be a fragmented, disorganized, and irresponsible jumble of words and phrases. Although there is no integration on the level of semantic or logical

relationships, it does in its way represent a tissue of associations connected by the recall of a succession of images. Sometimes it seems to be determined by an organization dependent upon perceptual and sensory response to the physical qualities of the word itself. This suggests that as the conscious focus upon ideational thinking is relinquished, for whatever reason, other levels of the thought process, having to do with memory, association, percepts, and sensory awareness, are exposed. This is a level of thought rarely exposed in language but present as part of ordinary mental experience. It does not cross the threshold of awareness but does provide the matrix from which images are differentiated.

We may approach this particular patient with a degree of confidence in our understanding of her way of thinking: She has an imaginative approach to the world which translates and interprets experience in the form of impressions, images, analogies, symbols. A natural development of this imaginative approach would imply an inner world of phantasy. Since she has lived her life in isolation and withdrawal, it is predictable that phantasy would acquire an increasingly convincing aspect and build a world judged by reality standards as delusional.

Language is a means of establishing contact with other people. The patient uses this mode to approach and to withdraw, to reveal and to disguise. This ambivalent use of language suggests a heightened sensitivity, uneasiness, and defensiveness in her relation to other persons. The inflexibility with which she imposes her own individual pattern on the conventions of communication would indicate a purposefulness and willfulness in her general make-up. The level and range of her vocabulary, the varied subject matter touched upon, indicate an originally intelligent, alert mind that received and stored vivid impressions and was easily stimulated by and responsive to her environment. She appears to have been strongly oriented toward the world of reality, to which her intellect and imagination add individuality and vitality. References to literature, the arts, foreign languages, place her as an educated and cultivated person. Her ability to manipulate language to express subtle criticisms, her play upon words, suggest a fair degree of intellectual sophistication. Wit and irony appear in her comments. The rhythm of her speech indicates an active and restless temperament.

These observations point to the personality traits that underlie a long-standing morbid process. Traces of this personality matrix are perceived in the language pattern only in fragmentary form. Something of the nature of the schizophrenic process can also be discerned in the language pattern. The language mirrors a progressive constriction to an overdetermined, unadaptive mode of representing reality and responding to reality. As she becomes progressively less interested, concerned, or distracted by other levels of thinking, she alternates between this intense, highly personalized, ideational transformation and, when less focused, the simple state of registering impressions, associations, and percepts.

Comment

In language, as in all expressive forms, several levels of meaning can be identified: First is the level of overt content, consisting of the consciously formed and articulated ideas and feelings that the speaker intends to communicate to the listener. Below this may be a level of implied meaning, latent content, suggested rather than clearly stated. The speaker holds this level of meaning in conscious awareness. He allows it to be perceived, but does not directly impress it upon the listener. A third level, the style, is not within the conscious intent, or even awareness, of the speaker. It is revealed in the form and manner by which he unconsciously selects and gives shape and substance to the content of his communication. These dimensions give language a psychological depth, in addition to a linguistic, logical, or semantic reality.

At the level of latent content, the schizophrenic patient's language often exhibits its most highly differentiated and individualized character. He generally adopts some form of symbolic transformation of meaning. This may be a form of imagery or a form of abstraction. The patient may also go to the opposite extreme, restricting his language to a formalized, mechanical, or literal pattern, devoid of personalized references and feeling tone. Both mechanisms deflect the recognition of the patient's private world of meaning. Sometimes there is an interplay of the two tendencies. This is also the level of double talk, ambiguities, hidden but implied meanings. The level of style reveals something of the patient's mental operation in selecting, defining, organizing, qualifying his perceptions of the outer reality of objects and the inner reality of ideas. Modes of thinking can often be better identified than the product of thought. A hypertrophy, and eventually a crystallization, of style occurs in the evolution of schizophrenic language pattern.

The schizophrenic patient is far less concerned with what he says than with what he means. The primary focus is on the meaning behind the word. The concern with the medium which conveys his meaning is of peripheral importance, and at times becomes negligible. Denotative function, explicitness, the codification of language into a universally accepted system of signs and symbols, all which characteristics underlie the accepted convention that language is primarily used for communication, is not given stress. Language appears to become a more plastic medium, by which meaning is pursued, explored, expressed, and only secondarily, if at all, communicated. The flexibility and malleability inherent in language come to the fore under conditions which demand that language encompass the world of personal and private meaning. This expressive quality of language can be identified to some degree in any form of language, but stands out with special clarity wherever the function of language becomes primarily concerned with the subjective inner world. This quality is found in poetry, and poetry cannot be understood by the same criteria as those applied to ordinary communication. A similar readjustment in perspective, to focus from overt content to latent content and style, may render schizophrenic language more intelligible.

As the function of language shifts from communications to self-expression, a parallel readjustment takes place in the level of thinking revealed by language. The focus on concise meaning, denotation, accepted signs, and institutionalized symbols, the conventional logic of relationships, recedes. Reverberations of meaning, intimations, explorations, states of awareness and responsiveness that have not as yet achieved definition and clarity are revealed.

So-called rational, conscious "thought" is only one final phase of the thinking process. This final form molds language into the semantic categories and syntax best suited to transmit its meaning. Transitional states of mental activity precede the formed, potentially articulate, "thought." Form and content are not so sharply defined, but are in the process of evolving. Complexes of ideational import may not be differentiated, or single aspects not yet synthesized. Symbols are still cloaked in the private and personal coloring of their origin. Abstractions are not completely divorced from the percepts and images, and have not undergone the process of synthesis that leads to concepts. Organization of relationships within the framework of sequence or inference possibly may not operate until the ideas themselves are formed and clear. This is the silent area of thinking, which language ordinarily does not attempt to convey. If this level of thinking is expressed in language, and is judged by the rules of logic and semantics, it must indeed appear bizarre, paralogical, ambiguous, or concrete, depending upon the segments that appear in the spoken words. Before a thought is realized and represented in language, it passes through a formative stage. If thinking be-

comes fixed, arrested, in this process of evolving, it may reveal itself in the stereotyped, bizarre, perseverating language pattern of the chronic schizophrenic patient.

Among schizophrenic patients there are always some who, despite their illness, are sensitive, intuitive, imaginative, and often creative, persons in potentiality, if not in actuality. These tendencies may become exaggerated and distorted but reflect the genuine endowment of the personality. Something of this appears in the sudden, astonishingly perceptive comments about inner experiences and events. These insights may be distorted in that they are projected into language as nebulous abstractions or a caricature of logic and syllogistic thinking, or fail to discriminate between image and idea. Yet one can still see their origin in potential assets of the personality, such as the capacity to symbolize experience through imagery or an aptitude for reasoning and abstraction.

Thought has content, but it is also an "event" or "process." Language obviously adapts itself to change in mental content. Less obviously, but observably, language adapts itself to the process of thinking by an alteration of its form and style. Discursive logical thinking, as part of intellectual operations, is readily carried through into language behavior. If thinking becomes focused on another level, that of perceptual organization, the structure and syntax of language will readily shift to literal or concrete appraisal. The relationship between language and thought in the first instance may be one of "communication," in which language becomes organized to convey ideas to another person. In the second instance the relation of language to thought may become one of "reporting" or "defining" reality as perceived by the speaker. The mind may be in a passive, receptive state, noting the flux of impressions, associations. If the person is encouraged to voice his inner experience, in other words, to free-associate, language will adapt itself quite differently than in the first instances. The relationship between the two becomes one of direct "expression." Impressions may be named, objects and people noted. The relational, discursive, structured aspect of language is replaced by a laxer system of notation. A person may be in an altered emotional state in which the imagination becomes stimulated. If he is intent on giving verbal expression to his mental, as well as emotional, experience, his language becomes flooded with images, expressed as metaphor, simile, and analogy. The relationship between language and thought has become one of "exploration." To take a last instance, in a person who is half awake, the levels of organized and directed thought subdued, the mind is subject to simpler principles of direct association, or to perception of sensory phenomena. If he has the impulse to talk, he may seize upon the physical aspect of the word, toss it about, make nonsense syllables, rhyme, form new word combinations. Here language becomes an "activity."

Generally we maintain a degree of flexibility which allows for readjustment of verbal behavior to accompany changes in mental and emotional experience. Yet every individual is to some degree restricted in this flexibility in that he has prevailing or dominant patterns of thinking which his general language style habitually reflects. The schizophrenic patient often shows a very distinct mental set, which is his characteristic approach to inner and outer experience. If the person becomes self-absorbed, withdrawn, engaged exclusively in his ruminations and speculations, he tends to use his most familiar and habitual mode of thinking. With decreasing flexibility of adjustment, a mental set can become automatic in its function and perhaps, finally, autonomous. Language, within limits, tends to adapt itself to represent emotional and ideational experiences. However, under ordinary circumstances a strong bias toward communication modifies the representational quality of language. Highly individualized and personalized intellectual, cognitive, imaginative, or emotional processes are not

directly represented in language behavior but become channeled, transformed, modified into conventionally designated patterns. The schizophrenic patient who lives in a perpetual world of privacy may make self-expression, or some function of language other than communication, the determinant of his language behavior.

Conclusion

This study of a chronic schizophrenic patient's language is presented as an illustration of aspects of language other than communication.

Language can be viewed as an expressive form which carries the imprint of the speaker. The configuration, structure, style, functions, and operations of his language identify the individual. This psychological dimension of language contains empirical evidence of mental processes and of the personality matrix in which they occur.

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Psychopharmacological Studies of Lysergic Acid Diethylamide (LSD-25) Intoxication

Effects of Premedication with BOL-128 (2-Bromo-d-Lysergic Acid Diethylamide), Mescaline, Atropine, Amobarbital, and Chlorpromazine

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One consequence of the recent interest in psychotomimetic drugs has been a search for pharmacological agents that will "block" drug-induced psychological disturbances and hallucinations. Fabing[1] reported that azacyclonol (Frenquel) in small doses prevented the occurrence of lysergic acid diethylamide (LSD-25) "psychoses" in man, although one of us (L. D. C.) was unable to verify this observation.[2] Other investigators have reported that LSD-25 intoxication is ameliorated by premedication with chlorpromazine,[3,4] serotonin,[5] and reserpine.[4] However, it has also been reported that serotonin[6] and reserpine[3] intensify LSD-25 effects. Hoch[7] found that premedication with amobarbital (Amytal) sodium and chlorpromazine did not prevent LSD-25 or mescaline intoxication but pointed out that such drugs produced suppressive effects when given at the height of the intoxication.

Several reasons exist for this confusing state of affairs. There has been a failure to distinguish between true pharmacological antagonism (blocking) and suppression. For example, in studying the effects upon the LSD-25 state of drugs with potent depressive action, such as amobarbital or chlorpromazine, one must differentiate between evidence of specific blocking from modest doses and masking or suppression secondary to impaired awareness in heavily premedicated subjects. Another source of difficulty is that LSD-25 intoxication is a complex condition, offering a wide variety of behavioral and psychological changes that may be observed and measured. When the object of the study is the modification of LSD-25 intoxication by other drugs, the choice made of what is to be measured may lead to appreciably different results. For example, if an investigator were to regard nausea as an important aspect of LSD-25 intoxication, he would probably find chlorpromazine to be an effective "blocking" agent. Other investigators emphasize the prevention of LSD-25 "psychosis" as though the latter were a predictable occurrence. This may be justified if one defines "psychosis" as the appearance of the typical LSD-25 perceptual disturbances. However, in our experience, psychosis in the sense of real behavioral disorganization occurs in only occasional experimental subjects given LSD-25 in the usual 1γ/kg. dose.

The experiments to be described in this paper were further attempts to assay the effectiveness of various drugs as blocking agents against LSD-25. Since there is little precise knowledge of the locus or mechanism of action of LSD-25, the choice of potential antagonists, while obviously guided by the experience of other workers, was frankly

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The LSD-25 and BOL-148 used in these experiments were supplied by Mr. Harry Althouse, of Sandoz Pharmaceuticals. The mescaline sulfate was supplied as a research grant from S. B. Penick & Company, New York.

speculative and arbitrary. Tap water was employed as a control. BOL-148 (2-bromo-*d*-lysergic acid diethylamide) was used, since it is structurally similar to LSD-25 but lacks the latter's hallucinogenic properties. Consequently, it was assumed that it might displace the LSD-25 at some hypothetical site of action in the central nervous system. On the other hand, mescaline sulfate, a drug with hallucinogenic activity similar to that of LSD-25, was given in the subhallucinogenic dose of 0.1 gm. on the assumption that this quantity might be sufficient to preempt a common site of action. Amobarbital sodium, 0.3 gm., as a central nervous system depressant, and chlorpromazine, 50 mg., as a tranquilizer-depressant, were studied as drugs which might be expected to antagonize the stimulating effects of LSD-25. Finally, atropine sulfate, 1.2 mg., was used as an autonomic blocking agent which might modify those aspects of the LSD-25 experience due to parasympathetic discharge. All medications were given orally.

Modest doses of premedication were chosen on the assumption that if true pharmacological antagonism occurred, as is exemplified by the model of nalorphine-morphine, such amounts would suffice to produce recognizable "blocking" effects. There were also other advantages in this choice. High doses of mescaline or atropine would have produced effects which could easily be confused with those of LSD-25, while excessive amounts of amobarbital or chlorpromazine would have obscured LSD-25 effects by producing nonspecific cortical depression.

The subjects were six medical students. A "double-blind" design was followed, so that neither the subjects nor the observers knew the exact order of the administration of drugs. All premedications were dispensed in 200 ml. of tap water to fasting subjects at 8:30 a. m., and LSD-25 was given at 10:00 a. m.

A modification of the extensive questionnaire for LSD-25 effects devised by Jarvik et al.[8] was completed by the subjects before the premedication, at 10:00 a. m., and 11:30 a. m. In addition, we made independent behavioral observations and mental-status evaluations at 15-minute intervals throughout each experiment. An effort was made to observe a broad spectrum of the physiological, perceptual, and psychological effects which may be produced by LSD-25. The subjects were also asked to record at regular intervals their perception of any somatic and psychological changes. These notes were later organized by the subjects into lengthy introspective reports.

The initial dose of LSD-25 was 1γ/kg. of body weight. However, after the first experiment this was reduced to 0.5γ/kg. There were two reasons for this change. First, one of the subjects experienced a severe "psychotic" LSD-25 reaction, which represented a real management problem. Second, it became apparent that the large dose produced such disruptive effects that the subjects were unable to complete the LSD-25 questionnaire accurately or to maintain an adequate introspective record of their experience. While there were minor differences from one subject to another, the smaller dose of LSD-25 produced mild but characteristic effects. These consistently included feelings of depersonalization, various paresthesias, a persistent urge to stretch, feelings of nervousness or general stimulation, and transient visual imagery when the eyes were closed. The effects of the larger dose were largely an extension of these effects, including more elaborate and persistent visual and somatic disturbances.

After three experiments, during which each of the subjects received three different premedications, a tabulation of the responses to the questionnaire and an analysis of the observer's protocols and the subjects' reports were made. With the possible exception of atropine, where fewer responses to the questionnaire occurred, the premedications failed to modify significantly any aspect of the LSD-25 intoxications. To check the significance of the observation on

atropine, three more experiments were run. All six subjects were studied under the influence of LSD-25 0.5γ/kg. alone, atropine 1.2 mg. alone, and atropine followed by LSD-25. These experiments failed to confirm the initial impression. Atropine did not decrease the response to LSD-25 but, instead, caused additional disagreeable autonomic effects, which actually made the experience more unpleasant.

Summary

Premedication with moderate amounts of BOL-148 (2-bromo-*d*-lysergic acid diethylamide), amobarbital sodium, chlorpromazine, mescaline sulfate, and atropine sulfate did not significantly influence the somatic and psychological disturbances induced by either large or small doses of lysergic acid diethylamide (LSD-25). There was no evidence of a blocking effect, such as might have been anticipated if these agents had any specific pharmacological antagonism toward LSD-25.

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Modifications of Oropharyngeal Bacteria with Changes in the Psychodynamic State

A Preliminary Study

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Although great strides have been made during the past 75 years in understanding infectious disease, there remain a number of unanswered questions, particularly relative to pathogenesis. For example, why do potentially pathogenic bacteria remain quiescent in the host's tissues for prolonged periods of time and then suddenly proliferate and cause disease? Why is it that one rarely sees 100% infection of a group of non-immunized, susceptible hosts exposed to the same pathogen? Many factors probably influence the interaction between host and bacteria. It is our working hypothesis that the host's psychodynamic state plays some role in this interaction. Other investigators have supported this hypothesis on the basis of psychologic observations.[1,5,6,8,11-13,16]

Dubos [2] has pointed out:

> Pathogens of all kinds . . . can persist in an active form in the tissues of a susceptible host, without causing detectable lesions or symptoms. These latent infections can remain symptomless for the lifetime of the infected individual, the host and the parasite ignoring or at least tolerating each other under normal conditions. Let the proper kind of physiologic disturbance occur in the host, however, and the equilibrium is upset. At times, probably, the parasite is eliminated altogether. More often, it starts proliferating in an uncontrolled manner, the latent infection evolving into overt disease. The problem of latent infection acquires large practical importance from the fact that most infectious diseases are caused by micro-organisms that are widely distributed among normal, healthy members of the population.

He pointed out that a variety of conditions can disrupt the host-parasite balance.

We are well aware that many factors besides emotions may influence the host-parasite balance, but these factors were not the main focus of this study. The purpose of this study was to investigate the effects of the host's psychodynamic state on the bacterial flora of the oropharynx.

The oropharynx is an important portal of entrance for many pathogenic micro-organisms. In addition, it is frequently the location of infections. It was thought that an investigation of the host's psychologic state concomitant with a survey of the bacterial flora of this area may provide clues to the role of emotions in the development of infectious disease.

There is an accumulation of evidence in the literature that emotions may produce a variety of changes in the naso-oropharyngeal system. The most extensive work on this matter has been done by Holmes, Goodell, Wolf, and Wolff.[8] They report changes of vascularity, secretions, and swelling of the mucous membranes of the nose with changes in the patient's adjustment to his environment. They felt that some of these changes could predispose the patient to the development of upper respiratory diseases. Fabricant [3,4] has described changes in the pH of nasal secretions of infants and children associated with crying and hyperventilation and changes in the pH of nasal secretions of adults with sudden fright.

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The investigation was done mainly during Dr. Kaplan's tenure of a Public Health Service Special Research Fellowship, National Institute of Mental Health, Department of Health, Education, and Welfare.

Starr [14] has found that emotions affect the pH of the saliva. Grossman and Brickman [7] have observed variations of salivary pH with varying conditions. Szasz [15] has described hypersalivation associated with unconscious oral sadistic impulses.

We considered it plausible to view the mucosa of the oropharynx as a frequently changing culture medium, the conditions of this medium depending upon its own secretions, the flow of secretions across it from the nose and mouth, and other conditions. As mentioned above, many of these factors are influenced by the subject's emotional state. Since implantation, growth, and proliferation of bacteria depend to a great extent upon the conditions provided by the culture medium, it seemed likely that the emotional state could influence the bacterial flora.

Methods

A series of bacteriologic and psychologic observations were made on a 32-year-old white woman during hospitalization on the psychosomatic unit of the Cincinnati General Hospital. This paper is a report of a carefully studied segment of this period and consists of 27 observations in which both types of data were obtained and evaluated.

The patient was seen and interviewed about five times a week by one of us (S. M. K.). The interviews lasted from 10 to 60 minutes. They were utilized for observation (in accordance with the research aim) and for the purpose of conducting psychotherapy. Each interview was completely tape-recorded, with the patient's permission and with the microphone within her sight. The interviews were typed, and the patient's verbal productions were studied for psychodynamic variables.* These variables were evaluated and roughly quantified, and a consensus was obtained between two of the investigators (S. M. K. and L. A. G.). No contrived "stressful" situations were attempted. Extensive observations of the patient's daily activity were made and recorded by the nurses. Psychologic tests were also obtained.

Each day the subject's oropharyngeal flora was studied by a microbiologist (D. E. F.) in the following manner: A sterile cotton swab was drawn across the patient's oropharynx. (We were fortunate that this procedure did not effect gagging in this subject.) The swab was then immersed in a small amount of saline and the diluent plated on blood agar. A differential colony count was made after incubation at 37 C for 18-24 hours. The total number of colonies counted varied between 150 and 200. Streptococci, Neisseria cocci, and staphylococci were the predominant bacteria. This report deals mainly with correlations between total streptococci and the psychologic content. Since unusually large numbers of beta-hemolytic streptococci were found at times, observations were also made of the patient's emotional state when this organism was abundant.

The Experimental Subject

The patient, a 32-year-old white, married woman, had a history of recurring bouts of upper respiratory infection and a history of rheumatic fever as a child. She could not recall having been concerned about this until the age of 22, when she developed "pneumonia." At that time her mother told her that the rheumatic fever she had during childhood had affected her heart. She was hospitalized for "pneumonia" at age 27, and, according to her report, the physician told her that she had rheumatic heart disease and that she would live for another 10 years only if she took good care of herself. In 1954, at the age of 30, she was hospitalized for hemoptysis, and a diagnosis of minimal bronchiectasis was made. The advisability of mitral commissurotomy was entertained. An exploratory thoracotomy was done because of the bronchiectasis and the cardiac valvular lesion. Stenosis of the mitral valve was found, and a commissurotomy was performed. After recovery, her emotional adjustment was poor, and she clung desperately to the hospital clinic and its doctors. She experienced multiple somatic symptoms and nervousness. She was referred to one of us for psychiatric treatment.

The patient, a moderately attractive and intelligent person, readily understood the purpose and method of psychotherapy. Her personal history revealed that she was angry and distrustful of her mother, with whom she lived. According to the patient, her mother had dominated her life and had made all her decisions for her.

A major complaint revolved around her mother's boy friend, who, she felt, spent too much time in their home, where he "ate and drank his beer." The mother took over this man's salary and handled his money for him. The patient said: "I dislike him, his weakness, his age, and he can't even manage his own money. They argue and fight. Mother is disgusted with him. He says I am jealous of the attention mother shows him. I used to be worried, afraid he would hit or kill her when he got drunk." The patient then expressed shame over her own unproductive, sick, complaining role

* The theoretical concepts of Dr. Thomas M. French [9] were adapted and used in the formulations of the psychodynamic "focal" conflicts in this case.

in life and her dependent attachment to her mother.

The patient did not know her real father, since he left home when she was very young. Her mother remarried when the patient was 2 years old. The patient reported that she was not aware of the fact that this man was her stepfather until the age of 6, when she learned it from a schoolmate. The patient had fond recollections of her stepfather, for she felt that he had been kind to her, and perhaps the most giving and understanding person in her life. On the other hand, these recollections were in sharp disagreement with mother's description of him to the patient. According to mother, he drank, stayed away from home, and mistreated the patient. The patient reported: "She said that when I was a baby he whipped me until I was black and blue and that she hated him for it." The patient did recall one occasion when her stepfather suddenly became angry at her, when she wore a dress that came above her knees. He yelled, "I don't want you to wear that dress again," but gave no further explanation except that she was a big girl and should wear dresses that covered her knees. She recalled that her mother and stepfather did not get along well, fought a great deal, and the fights often had to do with their sex life. The patient blamed her mother for the separation from the stepfather, which occurred when she was 16, and felt that her mother's behavior provoked the fighting. "I've seen her do things married women shouldn't do, go out with other men and drink."

The patient had one half-brother, several years younger than she. She believed that he was the favored child, and particularly favored by her mother.

The patient had been married twice, and in both instances the marriage was unsuccessful. Her first marriage occurred when she was 17, but it lasted for only a brief period. The reason she gave for the separation was that her husband beat her. She had a child by this marriage and felt guilty over the fact that she never took care of the child and completely relinquished the responsibility of raising him to her first husband's parents.

Her second, and current, marriage also was unsuccessful. At the time she entered therapy she was separated from her husband, and divorce proceedings were imminent. She had been dissatisfied with him and regarded him as uncouth, immature, and below her intellectual and social standards. She said she never loved him. Their sexual adjustment had been poor, and she was disgusted by his advances, his attitudes, and appearance.

During the hospitalization, when the mitral commissurotomy was performed, she became very attached to her doctors and particularly had an intense "crush" on the surgeon who operated on her. She would anxiously await his arrival and would be intensely disappointed if he did not visit her. She secretly hoped for a love affair with him.

Projective studies (Rorschach and Thematic Apperception tests) indicated that she was an egocentric, hysterical personality with a certain propensity for mood swings. On a deeper level, she was pleadingly dependent, still craving a closeness with mother, which she felt she had never had. She felt incomplete, unattractive, depreciated, and unloved. Her adjustment was further complicated by some vestiges of an irrational, arbitrary moral code, a feeling that it was wrong to try to make one's self modish or attractive.

Results

Dynamic Formulation During Observation Period.—During the period of observation the patient's main psychologic conflict involved exceedingly intense wishes to be given to and taken care of, but the direct expression of these wishes was inhibited by deep feelings of shame and guilt, since she felt greedy, unworthy of love, overdemanding, and infantile for having such intense needs. In addition to this intrapsychic conflict, her needs were bound to be frustrated, since they could not be satisfied completely in the hospital or, for that matter, anywhere. She attempted a number of types of solutions to her problem. The main solutions were as follows. She had hopes of gratifying her dependent needs through obtaining attention by getting punished. The punishment served to satisfy her feelings of shame and guilt and, at the same time, take care of some of her needs for attention. Her concept of herself was so depreciated that she felt unworthy of love unless it was diluted with abuse. Somewhat allied to this was her hope of being given to by appealing for attention and support for her physical symptoms and discomfort. She had been ill for many years and had been able to use physical symptoms in a plaintive manner to gain certain kinds of attention. Illness represented a setting in which she could extract care from others in a way less shameful to herself and somewhat more acceptable socially. Again, some suffering had to be endured through this means of dependency gratification.

Also closely related to the first solution above, and often fused with it, was the device of using sexuality to barter for dependent rewards. Her sexual concepts were highly masochistic, and her sexual wishes evoked feelings of shame. At times she attempted to deny her dependency or to utilize reaction formation. This was mainly in verbal form during the interviews rather than any attempts at an active behavioral level.

These solutions were not adequate because of the intensity of her needs, and consequently she felt frustrated. As a result of the frustration she felt over her dependent wishes, the patient experienced anger, but its expression was inhibited by the fear of further loss of potential sources of gratification of her wishes. The thought of expressing her hostility aroused her fears of desertion or loss of care from the therapist, hospital, and other sources of support. Her anger toward the therapist, therefore, tended to be turned in toward herself, projected, or displaced to others. During this period the displaced anger was not expressed directly to the person toward whom she felt anger, but it was described by her during the therapy hours.

During the course of therapy, her feelings of shame and guilt decreased, and she felt more secure about the relationship to the therapist and hospital personnel. Though the dependency conflict persisted, it diminished in intensity. During this period, simple wish-fulfillment dreams occurred, and also she was less fearful of loss of dependency from the hospital and the therapist; she was able to express hostility, sometimes displaced from the therapist, directly to the person toward whom she consciously felt angry (mainly nursing personnel).

With further therapy, shame and guilt over receiving from others continued to diminish. She learned, further, that anger could be expressed openly without jeopardizing her relationship with the therapist and the hospital, and her dependency wishes were increasingly gratified. She now used physical symptoms to demand care rather than to plea for pity. She evidenced some independent strivings (very minimal) that were not a total reflection of reaction formation, and she expressed feelings of increased self-esteem.

This repertoire of problem-solving techniques, of varying adequacy and effectiveness, was considered to represent the most important components of the psychologic material that was obtained. It was felt, after perusal of the first several interviews, that the shame over her dependency needs and the masochistic solution particularly correlated with high streptococcal levels. Also, conflicts over her hostility seemed related to fluctuations of Streptococcus counts. Initial correlations held true as further material was evaluated, and the other criteria fell into a logical order. An attempt was then made to quantify roughly, on a 0 to 4+ basis, the dynamic factors as they appeared in the individual interviews. The 0 to 4+ described intensity as it applied to and was not considered in terms of a trait in a universal population. For example, *this* patient during *this* span of interviews even at 4+ her self-esteem was not great.

The data were then aligned in a series of observations the Streptococcus from highest to lowest percentages, being arranged along the horizontal scale and ratings for each of these psychodynamic factors along a vertical scale (Fig. 1). A visual estimate of the correlation results from this synopsis of our observations. A statistical analysis of these data would not be warranted at this stage of our research.

Total Streptococcus Count.—The highest percentages of total streptococci were cultured from her oropharynx when these conflicts over dependency were intense and when the following cluster of solutions to these conflicts prevailed (Fig. 1): (1) obtaining attention by being punished; (2) handling her hostility, which was reactive to the frustration by projection and by turning it in toward herself; (3) using

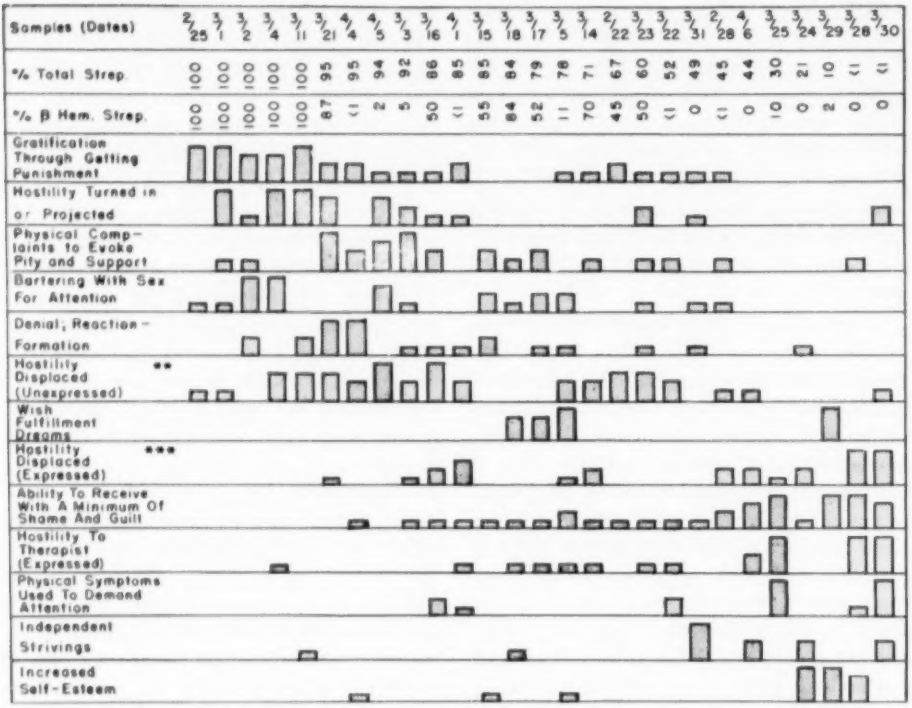
Samples (Dates)
2/25 3/1 3/2 3/4 3/11 3/21 4/4 4/5 3/3 3/16 4/1 3/15 3/18 3/17 3/5 3/14 2/22 3/23 3/22 3/31 2/28 4/6 3/25 3/24 3/29 3/28 3/30
% Total Strep.
0 0 0 0 0 95 95 94 92 86 85 85 84 79 78 71 67 60 52 49 45 44 30 21 10 11 11
% β Hem. Strep.
0 0 0 0 0 87 11 2 5 50 11 55 84 52 11 70 45 50 11 0 11 0 10 0 2 0 0
Gratification Through Getting Punishment
Hostility Turned in or Projected
Physical Complaints to Evoke Pity and Support
Bartering With Sex For Attention
Denial; Reaction-Formation
Hostility Displaced (Unexpressed) **
Wish Fulfillment Dreams
Hostility Displaced (Expressed) ***
Ability To Receive With A Minimum Of Shame And Guilt
Hostility To Therapist (Expressed)
Physical Symptoms Used To Demand Attention
Independent Strivings
Increased Self-Esteem

Fig. 1.—Representation of the total Streptococcus and beta-hemolytic-Streptococcus counts, in percentages, and the concomitant psychodynamic states.

Psychodynamic states are rated on a scale of 0 to 4+. The samples are arranged in order of highest to lowest. Total Streptococcus counts are arranged along the horizontal coordinate. Psychodynamic states are arranged generally along the vertical coordinate in order of decreasing intensity of neurotic conflicts (from top to bottom).

** Hostility to therapist displaced but not expressed openly to the object of displacement; reported, however, to the therapist.

*** Hostility to therapist displaced, expressed openly to object of displacement, and reported to the therapist.

physical symptoms to evoke pity and support; (4) using sexuality to barter for oral dependent rewards; (5) utilizing the psychologic mechanisms of denial and reaction formation, and (6) displacing hostility which she could not express to the object of displacement and could describe only during the therapy hour.

Streptococcal counts were lower after shame and guilt were diminished, (7) when dependent wish-fulfillment dreams occurred and (8) when hostility was more outwardly directed (but displaced to others than the therapist, such as the nursing and other hospital personnel).

The lowest percentages were obtained when the following cluster of adaptive mechanisms prevailed: (9) when the conflict was sufficiently modified to the point where the patient was able to receive without intense shame and guilt; (10) when she was able to express anger at the therapist openly when she felt frustration; (11) when she used physical symptoms demandingly rather than plaintively; (12) when there were evidences of independent strivings, and (13) when there were expressions indicating increased self-esteem.

The daily fluctuations of the percentage of streptococci are illustrated in Figure 2. There are essentially four phases. The first phase begins at the onset of the experiment (Feb. 22) and extends through March 11. This period is characterized by the many

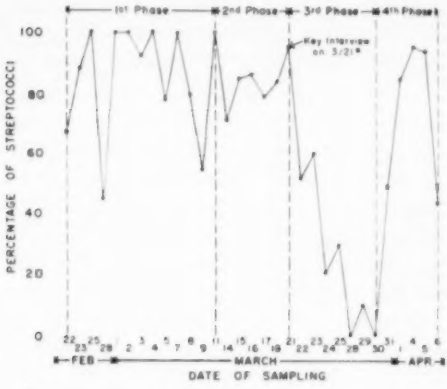

Fig. 2.—Total Streptococcus counts (percentages) during period of investigation.

* On this date the patient's shame and guilt about her dependent cravings were allayed and she was assured of prolonged care in the hospital as long as she felt the need of it.

days on which streptococci were the only bacteria obtained from the oropharynx. During this period the patient experienced the most intense conflict over her dependency wishes and the predominantly masochistic solution prevailed. Therapeutic efforts directed at reducing the intensity of the conflict were made during this period and seemed to begin to be effective in reducing the levels of Streptococcus counts in the second period, from March 11 through March 21. The third period, beginning March 21 and extending through March 30, is characterized by a marked decrease in streptococci. The most concerted attempts to reduce shame and guilt, to increase the patient's feelings of security in the therapeutic relationship, and to cater to her dependent needs were made on March 21 (Fig. 2).

On this day the patient began the interview by describing a number of physical symptoms and expressing dissatisfaction with her nonproductive role in life. Though she "wanted" to be more productive, she felt unable because of her symptoms. The therapist pointed out that there were no physical signs to account for her symptoms and suggested that, although she wished to be well, she was somewhat afraid of accepting good health. This was initially denied but led to her discussing why a person might have such opposing feelings. She recognized that she did gain attention and love from others through illness. A generalization was then made by the therapist, in a sympathetic manner, that people who have experienced deprivation in their early lives and prolonged illness, as she had, often discover this to be a useful means for gaining attention and love from others, but that she probably would not always be able to get affection on this basis. Then the therapist reassured her that she would remain in the hospital for an extended period of time and that she could look for a job when she felt ready and then remain in the hospital after going to work, during the difficult transition period. These comments were made at a time when her shame and guilt had been lightened considerably.

The interview of March 28, when the percentage of streptococci was lowest, was characterized by expressions of feelings of well-being. Her roommate had been discharged and she had the entire room for herself, and she experienced satisfaction in having been able to express her opinion and anger in an argument. She said she no longer felt like "a little speck of dirt."

The fourth phase began March 31 and was characterized by a rise in the Streptococcus percentage, which seemed related to the admissions of two new patients to the psychosomatic unit. This stirred her feelings of envy and fears of losing love and support.

Beta-Hemolytic Streptococci.—Beta-hemolytic Streptococcus colonies were differentiated from alpha- and gamma-Streptococcus colonies and counted separately. Typing was not possible. The patient had a history of rheumatic fever and frequent throat infection; and since this organism is associated with these disease states, a comment about their presence seems worth while.

Beta-hemolytic streptococci were present in large numbers at the beginning of the

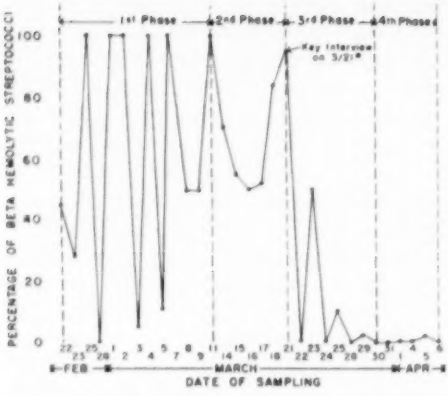

Fig. 3.—Beta-hemolytic Streptococcus counts (percentages) during period of investigation.

* On this date the patient's shame and guilt about her dependent cravings were allayed and she was assured of prolonged care in the hospital as long as she felt the need of it.

observation period (Fig. 3). The number fluctuated widely, from none to 100%. It is of interest that there were times when the colony growth was exclusively of beta-hemolytic streptococci and yet no symptoms or signs of infections appeared. Very high levels of beta-hemolytic streptococci occurred on those days when the dependency conflict was intense and the attempted solution was of the masochistic type.

Comment

This paper is presented as a pilot study and indicates a correlation of the psychodynamic state and certain bacterial flora of the oropharynx. It reports an initial attempt to study some aspects of the pathogenesis of infectious illness at a psychodynamic, as well as a bacteriologic, level. The experiment was essentially an "open" one. There were no prior indications to suggest the selection of any particular psychodynamic constellation to compare with the bacteriologic findings.

In this case the percentage of streptococci grown from a swabbing of the subject's oropharynx was highest when her intense oral dependent wishes were frustrated because of her shame and guilt and the realistic limitation imposed by her environment. She reacted to such frustration with anger, but the anger had to be inhibited, since she considered open expression as threatening to her dependency relationships. During these periods she sought dependency gratification through masochistic and other means. As the conflict diminished in intensity, the Streptococcus percentage diminished. The relative percentage of Streptococcus bacteria was lowest when shame and guilt were diminished, when her environment offered additional gratification of her needs and she was able to accept them, and when she could direct her hostile feelings outward.

Seemingly, the more intensely she experienced this conflict and the more pathologic the defense mechanisms, the higher the precentage of streptococci. It is difficult to pick out one specific psychologic factor (if there is one) to associate with the Streptococcus level. Is it the intensity of the dependent yearnings, the extent of the shame, the unexpressed rage over the frustration she felt, or the type of solution attempted? This cannot be delineated; but, rather, the relevant psychologic variable appears, from our preliminary study, to be a psychodynamic cluster of interrelated factors.

An increase in streptococci cannot be considered necessarily as the precursor of an upper respiratory infection. Of interest, however, is the similarity of our findings to those already described by others. Saul[12] reported an investigation of a series of patients who experienced repeated bouts of coryza, sore throat, laryngitis, and other symptoms. These patients were in psychoanalytic treatment. Our findings were established completely independently of his; yet they are quite similar. Saul stated:

> The central observation is the occurrence of colds in these patients in situations of thwarting of very strong receptive demands, expressed largely but not exclusively, in oral terms, with consequent rage, or with intensification of hostility from other sources, such as narcissistic rivalry. These receptive desires were not fully conscious to the patient, but were mostly excluded from consciousness be-

cause of shame, guilt, or similar reasons. . . . Some of the material suggests that the coryza may be in part a defense reaction against unacceptable, more or less masochistic unconscious receptive wishes or fantasies, just as physically it is a defense reaction against invading foreign agents, such as physical irritants or micro-organisms.[12]

Grinker and Robbins[6] have commented: Upper respiratory infections in the nasal and pharyngeal passages very frequently occur after situations or fantasies which threaten the subject's dependent attachments. Perverse sexual acts such as fellatio or hostile and envious oral fantasies may stir up anxiety and fear of losing a needed relationship.

In his experiment in the substitution of symptoms by hypnosis, Seitz[13] reported: "Some findings of the present experiments suggest that infectious diseases may occur as substitute reactions for hypnotically removed psychogenic symptoms." During the experiment, pleurisy occurred on one occasion and bronchopneumonia on another when Seitz frustrated the patient's (the patient weighed 325 lb.) oral-intaking wishes by removal of the defense of overeating. This seemed to encourage a great deal of reactive rage, which was not verbally expressed. It should be pointed out that other symptoms occurred when overeating was blocked. However, while the patient was at times successful in finding a substitute symptom, the infectious diseases may have reflected a failure to find a satisfactory substitute.

In his study of patterns of somatic displacement, Kepecs[10] reports the occurrence of a "sore throat" (diagnosed as allergic) in a patient when the patient's feelings and ideas came closer to the surface. In this instance the feelings which were of intense anger were blocked from expression. The symptoms abated when they were expressed during the following therapy session.

We are carrying out further experiments, utilizing "blind" techniques, in an attempt to validate our present findings. Additional modifications in both the bacteriologic and the psychologic methods have been developed, with particular attention paid to the evaluation of the reliability of these methods.[9]

Summary

There are a number of questions relating to the etiology and pathogenesis of infectious diseases. Pathogenic bacteria may lie dormant in the tissue of the host for prolonged periods of time and suddenly proliferate and infect when the host-parasite balance is disturbed. The investigators have sought to determine whether emotional factors can play a role in the host-parasite relationship and balance by studying the association between the host's psychodynamic state and the bacterial flora of the oropharynx.

The oropharynx can be thought of as a culture medium whose conditions change, to some extent, on the basis of the subject's emotional state, as well as in reaction to other factors, and these changes can influence microbial implantation, growth, and proliferation.

An evaluation was made of the psychodynamic state and the bacterial flora of the oropharynx of a 32-year-old woman who had a history of recurrent upper respiratory infections and rheumatic fever. There were no prior hypotheses as to what psychodynamic states might be associated with high Streptococcus counts.

The findings strongly suggested that the percentage of both total Streptococcus and beta-hemolytic Streptococcus colonies cultured from her oropharynx varied with her psychodynamic state. The percentage of both varied directly with the ways in which the patient handled her intense dependent yearnings. The direct expression of these wishes was inhibited by deep feelings of shame and guilt. The hostility reactive to such frustration was inhibited from expression because it aroused fears of desertion and loss of affection from the therapist, hospital, and other potential sources of gratification of her wishes. When the patient attempted to gratify her dependency needs in ways which brought her punishment or enhanced her suffering, the total Streptococcus and beta-hemolytic Streptococcus counts tended to be very high. When she

attempted to gratify these dependent urges without using masochistic devices and when she found herself a more worth-while and acceptable person, these counts were relatively low.

The significance of these findings and plans toward their validation are briefly outlined and discussed.

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Books

BOOK REVIEWS

Psychosynthesis: A Project for a Scientific Psychology. By John P. Crawford. Price, $4.00. Pp. 104. Ash & Company, London, 1956.

This privately printed small volume is a curious production. It purports to be a thesis or synthesis, but nowhere is this realized or even attempted. Even in the last chapter there is no summary or hint of synthesis. Nevertheless, this book is considered worthy of a review notice because each chapter is filled with abstractions from an incredible number of references. The book as a whole cites several hundred authorities. The chapter titles are as follows: "Sleep and Consciousness"; "Mood and Feeling"; "Energy, Metabolism and Tone"; "Perception, Memory and Imagination"; "Attention, Concentration and Learning"; "Growth, Maturity and Decay"; "Instinct and Development"; "Environment: Past, Present and Future," and two clinical chapters. There is no index.

ROY R. GRINKER, M.D.

Tranquilizing Drugs. By Harold E. Himwich, M.D. Price, $5.00. Pp. 205. The American Association for the Advancement of Science, 1515 Massachusetts Ave., N. W., 1957.

Alcoholism, Basic Aspects and Treatment. By Harold E. Himwich, M.D. Price, $5.75. Pp. 220. The American Association for the Advancement of Science, 1515 Massachusetts Ave., N. W., 1957.

These two volumes are publications 46 and 47 of The American Association for the Advancement of Science, and both are ably arranged and edited by Harold E. Himwich. They contain papers presented at symposia held at the Association's Atlanta, Ga., meeting December, 1955. Each includes an introduction by Chauncey D. Leake. It is obvious that symposia, including fourteen and nineteen papers, respectively, cannot be summarized, although the last presentation in each volume contains such a summing up by Himwich. It can only be stated that each volume contains the significant information available at the time presented by the most competent investigators of the subjects discussed.

ROY R. GRINKER, M.D.

Closed Ranks: An Experiment in Mental Health Education. By Elaine Cumming and John Cumming. Price, $3.50. Pp. 192. Harvard University Press, Cambridge 38, Mass., 1957.

The authors, a sociologist and a psychiatrist, with support from the Commonwealth Fund, New York, set out to test attitudes toward mental health and illness of the population of a small town in Canada, attempt six months of mental health education, and then retest the population. The fascinating story of the investigators' and teachers' experiences with the townsfolk before and after the educational period should be read in detail. According to informally expressed opinion and objectively revealed test material, the educational experiment failed in its goal of changing the population's attitudes toward mental illness. The experiment raised anxiety and hostility without changing attitudes. The study was a success, however, in the amount of information culled and in the constructive experiences which helped the authors in subsequent educational ventures. One conclusion was missed by this reviewer: the incapacity of any persons to learn in a highly charged area without personal emotional participation. Didactic discussions, lectures to lay persons with or without audiovisual aids are universally sterile unless motivational participation can be counted on. A small working group engaged in ventilating processes within themselves or in relation to persons close to them is more facilitative toward change in attitudes than a year of lectures. This is a fascinating, well-written story, and psychiatrists interested in public mental health should not fail to read it.

ROY R. GRINKER, M.D.

Les Mécanismes cérébraux de la prise de conscience. By P. Chauchard. Price, $4.75. Pp. 240. Masson & Cie, 120 boulevard Saint-Germain, Paris, 6e, 1955.

In examining the problem of human consciousness and insight, the author aims to integrate the neurophysiological orientation with the views of Pavlov and the psychoanalytic schools and to inflict a *coup mortel à l'idéalisme dualiste*. Special emphasis is placed on the chronaximetric studies of Lapicque and the metabolic origin of electrical properties of neurons. The concept is advanced that the characteristic excitatory properties of each neuron and the variations in these states of excitation modify the impulses acting upon the neurons so as to enhance and inhibit the incoming impulses. Furthermore, individual neurons, acting in concert with one another, have fluctuations in their chronaximetric status. On this basis there is elaborated Pavlov's concepts of the conditioning process through which the reactive patterns of the organism are developed. There is discussed the relative influence of genetic and experiential factors in patterning of behavior. The formulation is presented that in those animals, and especially man, whose behavioral system is least developed at birth the factors of experience and conditioning play a greater role than in those organisms which, being closer to maturity at birth, have more rigidly species-defined behavioral pattern. The regulations of the behavior are conceived of not as being localized in special areas but as resulting from the interactions of the various portions of the nervous system. Having explored the observations derived from electroneurophysiology and from Sherrington's and Pavlov's experimental techniques, the author expresses the point of view that there is no disparity between these groups and the concepts of dynamic psychiatry (without regard for the minor individual differences among the various schools). A reflective awareness of one's self, the domain of analytic psychiatry, is conceived of as another aspect of behavioral autoregulation, as elaboration of the more primitive and stereotyped regulatory functions of the nervous system. There is developed a unified theory of behavior, often supported by data collected from the author's experiments and from the literature.

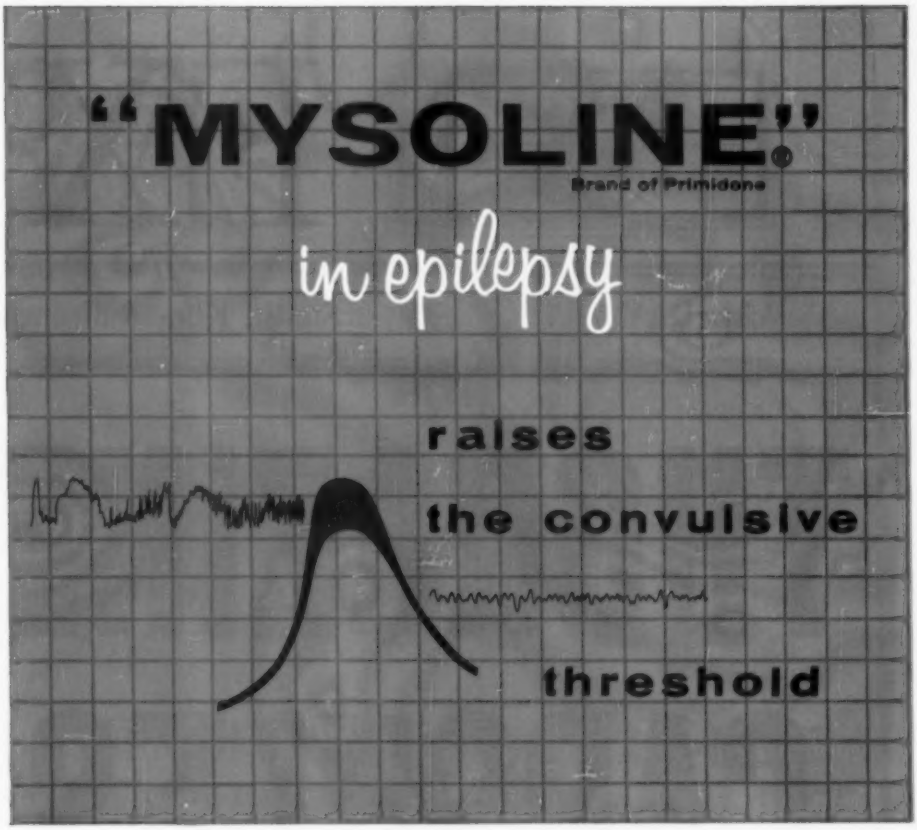
There are, however, many lacunae where the theoretical system remains unsupported by evidence, and here the questions raised provide the challenge to find new evidence to support the theoretical structure or to reconstruct it.

PERCIVAL BAILEY, M.D.

Announcements

A clearinghouse of information on psychopharmacology is being established by the Psychopharmacology Service Center of the National Institute of Mental Health. An extensive collection of the literature in this field, including pharmacological, clinical, behavioral, and experimental studies of the ataraxic, psychotomimetic, and other centrally acting drugs, will be classified and coded to enable the staff to answer a wide variety of technical and scientific questions. As soon as enough materials have been assembled, the Center plans to offer bibliographic and reference service, as well as the preparation of critical and analytic reviews of special topics in the field.

In order to accelerate the growth of the literature collection, the Center invites persons working in this field to provide three copies of any papers that deal with their work—whether reprints, prepublication manuscripts, progress reports, informal mimeographed reports, papers read at meetings, or abstracts. Letters outlining work in progress would also be welcome. Any restrictions that authors may wish to place on the Center's use of their papers will be strictly observed. All materials should be addressed to the Technical Information Unit, Psychopharmacology Service Center, National Institute of Mental Health, 8719 Colesville Rd., Silver Spring, Md.



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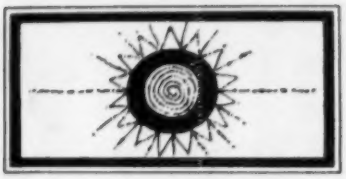

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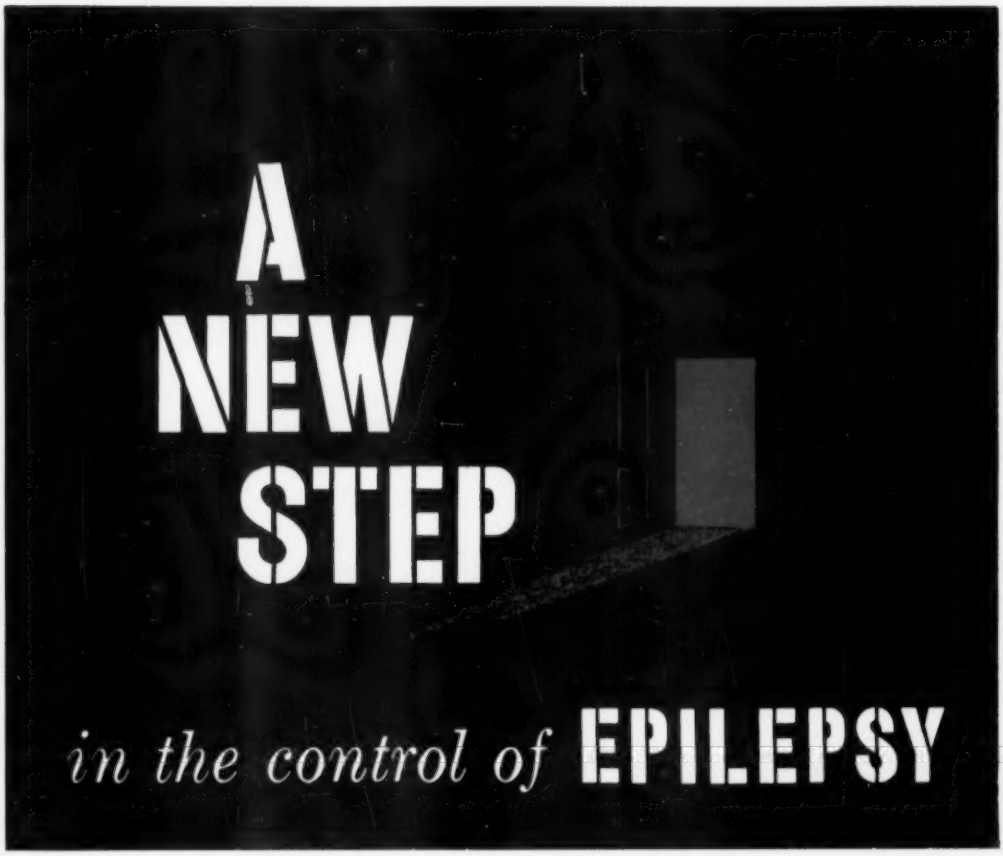

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2. Bergstrom, W. H.; Carzoli, R. F.; Lombroso, C.; Davidson, D. T., and Wallace, W. M.: A.M.A. Am. J. Dis. Child. 84:771 (Dec.) 1952.

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1. Sainz, A.: Personal communication.
2. Hutchinson, J. T.: Evaluation of Pacatal in Psychotic States, address before the American Psychiatric Association, Nov. 16, 1956.
3. Bowes, H. A.: Am. J. Psychiat. *113*:530 (Dec.) 1956.

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